B. SHUBIN and Yu. GRITSMAN

Men vs. cancer

MIR PUBLISHERS
MOSCOW

Cancer is one of the most acute problems that exist in world biology and medicine. It is being tackled by a vast number of scientists and practitioners.

Two specialists in the field, both Doctors of Medical Science, wrote this book. Complex questions are made more comprehensible because they are dealt with from the point of view of the founders of different directions in oncology. Achievements in this field along with the problems still existing are described, and the numerous legends and myths are countered by true stories about the successful treatment and prevention of this formidable disease.

The book is intended both for a wide circle of readers and for medical specialists interested in the problem of cancer.

MEN vs. CANCER

Б. ШУБИН, Ю. ГРИЦМАН

ЛЮДИ
ПРОТИВ
РАКА

ИЗДАТЕЛЬСТВО
«СОВЕТСКАЯ РОССИЯ»
МОСКВА

B. SHUBIN and Yu. GRITSMAN

Men vs. cancer

MIR PUBLISHERS
MOSCOW

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Arthur Aksenov

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TO THE READER

Mir Publishers would be grateful for your comments on the content, translation and design of this book. We would also be pleased to receive any other suggestions you may wish to make.

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Foreword

I have the pleasure of prefacing B.M. Shubin and Yu.Ya. Gritsman's book, *Men vs. Cancer*.

The authors are well-known Moscow oncologists who wrote this original work in which scientific descriptions and deductions concerning the treatment of malignant tumours are interspersed with stories about such celebrated physicians as A.P. Chekhov, P.A. Herzen, N.N. Petrov, L.A. Silber, S.P. Fedorov, etc. By introducing the reader to this close circle of some of the founders of science, they make it easier to comprehend certain scientific theories which at times may be very complicated.

This book deals not only with the successes of modern oncology but also with the difficulties of concern to all people, which arise in uncovering the mysteries of cancer.

It is also important that the authors simultaneously analyze the sources of quackery in medicine. The exposure of falsehood in science is vital for getting at the truth, but in medicine, particularly in oncology, this is most essential because the issue involves saving human life. Thus, the unmasking of charlatans becomes a task of social significance.

This work throws light on many other no less important questions: the interrelations of doctor and patient, and of doctor and the society he protects from diseases; it introduces us to the scientific discussions and clashes of opinion taking place between scholars and practitioners, etc. All this is presented in a very interesting manner and based on a wealth of material. Throughout the work, the reader becomes aware of the progressive views of the authors on these subjects.

I am convinced that the reader will find much that is of value in this book.

N.P. Napalkov,
Academician, AMS, USSR
Chairman of the USSR Society
of Oncologists

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Reading Chekhov Anew

Arthur Clarke, author of the futuristic book, *Profiles of the Future*, was once asked what he, as a well-known science-fiction writer and scholar, would wish to learn from the inhabitants of other planets possessing higher intelligence, if he ever had such an opportunity.

"I would like to know whether space and time are finite or infinite," replied Clarke. "Does death always accompany life?" Then he added: "On second thought, I would prefer to know how cancer can be defeated..."

Heightened interest in oncology is not merely stimulated by the widespread incidence of the disease and its frequently fatal outcome, but also by the very mystery inherent in the word "cancer".

The name of the disease is attributed to Hippocrates, who observed it as far back as the fourth century before our era. Approximately one and a half thousand years after Hippocrates, the great healer of ancient times, Avicenna, in his famous system of medicine, *The Canon of Medicine*, provided the following explanation: "...It seems that this disease is called cancer due to one of two circumstances, either because it seizes an organ like a crab grasps its prey, or because of its form..."

The earliest theories concerning the origin of cancer are also linked with these outstanding medics. Hippocrates, for example, explained that the first appearance of cancer, as of other serious diseases, is caused by a disturbance in the proportions of the main fluids of the body: blood, mucus, yellow and black bile. (A few centuries later the Greek physician, Galen, firmly asserted that acrimonious women are predisposed to tumorous diseases.) According to Avicenna, scirrhus, the hard form of cancer, may develop from inflammation—a phlegmon, erysipelas or an abscess. Although these theories may seem naive in comparison with contemporary viewpoints, knowledge about cancer was so negligible as to have been practically useless. Nevertheless, the existence of this knowledge is in itself remarkable. It indicates that even at that time malignant neoplasms were not a subject for casuistry. Rather, just as with any naturally occurring phenomenon in medical practice, it was essential to clarify the causes for their occurrence.

In past times, case histories were, of course, not recorded. However, there is unquestionably "documented" evidence that cancer had been encountered a very long time ago.

Nearly 350 years ago Rembrandt depicted a woman on one of his canvases who was obviously stricken with breast cancer. The tumour can be seen with the naked eye.

The woman sits warming herself by a stove with an expression of doom on her face.

A human bone found in the earth also provides objective evidence. It is not only a symbol of the grave (no wonder the generally accepted warning of danger to life is the representation of a skull and crossed bones). A human bone is also evidence of life that existed at some time. Remember Hamlet's monologue over the skull of Yorick, the king's jester?

Human remains reveal much about the people who have lived at certain times in the past. The study of fossilized bones made it possible for M.M. Gerasimov, the famous Soviet anthropologist and sculptor, to reconstruct the external appearance of our distant forefathers, and for the Leningrad roentgenologist Professor D.G. Rokhlin to learn a great deal about the diseases from which they suffered. Professor Rokhlin succeeded specifically in defining a number of tumorous lesions of the bones. For example, roentgenograms of the skeleton of a 40-45 year-old female, who lived more than three and a half thousand years ago, revealed changes typical of cancer metastases in the bodies of the second cervical and several thoracic vertebrae.

It is not possible to determine precisely the source of metastases by means of roentgenograms; however, since the case above was that of a female, one may assume, within a safe margin of error, that she suffered from cancer of the breast, because bones are a common location of breast cancer metastases.

It appears that the patient had been bedridden and unable even to turn her head. Bearing in mind the medical aid available in those times, one can only imagine what this woman suffered.

Thus, it is established that humans have encountered malignant tumours since times immemorial. Why then has the problem of cancer prevention become so urgent in recent years? To what extent did it concern people at the dawn of our century?

In order to investigate the issue we could peruse the specific literature. However, it would be even simpler to take a book by Anton Chekhov from the bookshelf and reread it from a new point of view.

It is clear why Chekhov is the logical choice: he was a physician and made wide use of medical topics in his works. It must also be noted that he was not just a rank-and-file doctor, but a highly educated specialist of his time.

Chekhov's joke, where he professed that medicine was his lawful wife and literature a mistress, has been widely quoted. This, however, was that rare case where the love affair caused no harm to the marriage, which, in turn, enriched love with new content.

"My interest in medical sciences greatly influenced my literary activities, " Chekhov wrote in a short autobiography. He repeatedly emphasized the importance of science and the scientific method for a physician. "Knowledge is foremost in medicine, philanthropy comes after; without knowledge, medicine is quackery" (from the story "The Tedium of Life").

The Soviet internist, G.P. Shultsev, considers Chekhov one of the outstanding Russian physicians at the turn of the 19th century. This opinion was shared by the late Academician I.A. Kassirsky. In addition, Academician S.S. Yudin, one of the founders of Soviet surgery, named Doctor A.P. Chekhov among such eminent doctors as N.I. Pirogov, S.P. Botkin, I.M. Sechenov, N.V. Sklifosovsky, S.P. Fedorov, N.A. Velyaminov and S.I. Spasokukotsky.

Chekhov's stories are delicately interwoven with his deep and versatile knowledge of medicine. Although he has said that he depicts patients only because they happen to be "characters" as such, or because they are picturesque, descriptions of different diseases may be encountered in his stories. Cancer is described in only three of his works, or rather, more precisely, in two. In the story "Gooseberry" the death of the hero from a tumour of the stomach is found only in the author's original sketches.

In "Grasshopper" Dymov performs an autopsy on a patient who suffered from malignant anaemia and finds carcinoma of the pancreas.

A patient suffering from cancer is described in greater detail in *Three Years*. It is remarkable that when Chekhov edited this story which had been planned as a novel, he made considerable reductions in the text but nonetheless preserved most of the details concerning the diseases which the characters suffered from.

Let us recall the plot of the story.

Aleksei Laptev, the son of a Moscow millionaire merchant, is hopelessly in love with Julia, the daughter of a provincial doctor. Having made up her mind that marriage to a decent, well-educated, kind man who loves her is bound to bring a change in the dull life she is leading with her wayward and selfish father, Julia, who had at first turned down her suitor, finally consents to be his wife.

After the wedding both young people realize what a terrible mistake they have made, and suffer endlessly.

They live surrounded by their suffering relatives: Aleksei's blind and abandoned father, founder of the haberdasher's firm "Fedor Laptev and Sons", his brother, who has lost his mind, and sister Nina, who is dying from cancer of the breast. It is her case history that we shall examine.

Nina is not yet forty. We first encounter her in the story after an operation for the removal of a breast. She lives in a quiet provincial town (cows are sometimes herded by her window), however, the town is probably fairly large, because there are 28 doctors practicing in it. This is an impressive number for those times if we take into account that in all of Russia in 1894, when the story was written, there were only 12 500 medics and they were concentrated in St. Petersburg (1500) and Moscow (1000). In rural communities, on the average, there was only one doctor for every 33 000 inhabitants, but in some provinces one doctor would have to provide aid to fifty thousand or more. (For the sake of comparison, it might be noted that in the USSR today the annual graduation class of physicians is more than two times the total number of doctors that were practicing in Russia when Chekhov lived.)

But let us return to the story.

To perform such a simple operation on Nina, a specialist had to be brought from Moscow. The local physicians had refused to operate. Although sufficiently skilled, they feared for their reputations.

As far back as the middle ages, the British surgeon, John of Arden, advised his colleagues to avoid operating malignant tumours for the same reasons. In all likelihood the doctors who were caring for Nina had never heard of the British doctor and his advice, but they knew from their own experience that oncological diseases usually came to a very sad end.

Nina's fate was no exception to the rule: she grew visibly frail and weak and everyone expected a relapse.

In Chekhov's notebook we find references relating to his story *Three Years*:

"Is it impossible to prevent a recurrence?

"Her father, a physician, shrugged as if to say that doctors are not gods..."

A few months later the relapse occurred.

"She was so pale that she seemed lifeless, particularly when she was lying on her back...", the writer describes the patient.

Chekhov also shows how Nina's mental state gradually changed as the disease progressed.

At first she fully understood her condition and knew what awaited her: "Of course, when death approaches, neither prayers nor doctors will help..."

But when she began to feel better one day, she got up from bed, dressed and suddenly became convinced that she would recover. And much later, when she was already very ill, "despite acute pain, Nina began imagining that she was getting better. She got out of bed every morning, dressed as if she were quite healthy and lay on the bed in her clothes all day long".

As a physician, Chekhov knew well the symptoms of malignant tumours. In 1900 when Menshikov, a journalist, asked Chekhov what disease Lev Tolstoi was suffering from, he replied that it was not cancer, because cancer affects the appetite, the general condition, before all else, but the main thing is that "the face is a give-away in the case of cancer; it is more than certain that Lev Tolstoi is healthy... and will probably live another twenty years".

In his story *Three Years* Chekhov casually touched upon the fundamental question of oncology. The husband of the patient reproached local physicians for showing no interest in the case, for not knowing anything about cancer and what causes it.

Indeed, what was known about cancer at the time when Chekhov was writing this story?

More than a hundred years had elapsed since Dr. Percivall Pott, the surgeon of a London hospital, had described cancer in chimney-sweeps, an occupational disease caused, in his opinion, by the continuous effect of soot on the skin. Pott's hypothesis, however, was long in finding confirmation. It was only in 1915 that Japanese scientists K. Yamagiwa and K. Ichikawa succeeded in inducing skin cancer in rabbits by means of coal resin. This marked the beginning of research on chemical carcinogens.

Microbiologists A. Borrel and F. Bosk had not yet voiced their assumptions regarding the possible viral origin of tumours. They wrote about this hypothesis in 1903. Seven years later Peyton Rous offered proof supporting their hypothesis in experiments on chicks; after another fifty years this

87-year-old American researcher won the Nobel prize.

At the time the story *Three Years* was published Lev Silber had just been born; he became an academician and won fame as an outstanding Soviet microbiologist, immunologist and virologist, founder of the modern virogenetic theory of cancer.

During the latter half of the 19th century two hypotheses were dominant in oncology. The "stimulation theory" advanced by R. Virchow, according to which tumours appear as a result of the proliferation of tissues due to chronic inflammation, and Yu. Kongeim's theory of "embryonal germs" which contends that a tumour is the consequence of a defect in intrauterine development. Incidentally, the latter theory does not exclude the former, because chronic inflammation may give rise to tumoral growth of abnormally situated embryonic cells.

Virchow's theory, which dates back to the era of pre-experimental oncology, is based on numerous observations made by physicians of all specialities where cancer was found coupled with chronic inflammatory processes. Although it was later clarified that inflammation is not necessarily an essential link in the chain of phenomena leading to tumour growth, this theory dominated the minds of scholars for 80 years.

Chekhov was undoubtedly acquainted with Virchow's tumour theory which was published in 1867. He highly respected this German pathologist and in a letter to the publisher A.S. Suvorin ranked him on a level with his own teachers N.I. Pirogov, S.P. Botkin and G.A. Zakharyin.

Nevertheless, one must give credit to Chekhov's insight that he realized how complex and vague the explanations regarding origin of cancer tended to be. When Nina's husband, one of the characters in the story *Three Years*, tried to explain what cancer actually is, Chekhov remarked with irony: "He was a know-it-all of all sciences." Nina alone was convinced that her unfortunate love was the cause of cancer.

The most outstanding discoveries in oncology were yet to be made. It was not by chance that in Chekhov's time this science was just beginning to develop: not cancer, but another disease was responsible for the greatest mortality among the population.

In his literary works and letters Chekhov writes about cancer much less frequently than about consumption, or tuberculosis.

In Chekhov's last story "The Bride", the pale thin student Sasha, who is always coughing, dies from tuberculosis. The wife of the main hero of the play *Ivanov* undergoes treatment with no success; in the story "Gusev", soldiers returning home from the Far East are travelling in the sick-bay of a ship, gasping for breath, because they are suffering from the last stage of consumption.

The author's anger rings in the words of one of the characters of his story: "How could severely ill patients have been placed aboard a ship in suffocating heat, tossed about by the waves, instead of being treated in a hospital, on land, in peace and quiet? Death threatens you in such conditions, but your attending physicians shipped you off in order to get rid of you. Such doctors have no conscience, no humanity..."

To be sure, the soldiers succumbed to the monstrous conditions and died. One after another their bodies were sewn into sailcloth bags and committed to the sea depths.

Chekhov's frequent focus on tuberculosis cannot be explained simply because he himself eventually fell victim to this disease. In "Late Flowers", a story Chekhov wrote when he was quite healthy, Marusya Priklonskaya died from consumption. At that not too distant time, consumption was a common and merciless disease. Even the cholera epidemic of 1892 (Chekhov, as a rural doctor, took part in its eradication) caused 300 000 deaths, but proved to be less devastating than the annual toll taken by tuberculosis. When an outbreak of the plague was feared in Russia in 1897, Chekhov wrote to Suvorin: "... as it is, to say nothing of the plague, in our country barely 400 people out of 1000 survive to five years of age, while in the rural and urban localities, in the factories and back streets you will not find a single healthy woman."

Incidentally, confirmation of Chekhov's opinion regarding the predominance of tuberculosis as a cause of mortality among the population may be found in Brockhaus and Efron's encyclopaedic dictionary published at the turn of the 19th century.

In Russia, the system of state-sponsored antituberculosis programmes was barely in its infancy. The first specialized out-patient clinic was opened in Moscow in 1904. Ten years later, in such a vast country as Russia, only 67 small out-patient clinics and a few sanatoria were functioning that could barely accommodate 2000 patients.

Malnutrition and hunger, to a great extent, promoted the spread of tuberculosis (the geographic distribution of both evils coincide exactly). It is not surprising that in his story "Oysters" Anton Chekhov labels hunger "a strange disease" which one cannot find in textbooks, but against which half the world population is still not insured.

"...I feel no pain but my legs buckle under me, words stick in my throat and my head lolls helplessly to one side..."

Quite understandably, in a letter to the secretary of the editorial board of *Oskolki* V.V. Bilibin, Chekhov wrote that in "Oysters" he was "testing himself as a medicus".

Tuberculosis, severe infections and high infant mortality made short shrift of human lives. These are the factors that predetermined the primary tasks of medicine. With the growth in social and economic progress and the accumulation of knowledge, the successes of medicine multiplied and this led to an increase in the human lifespan.

In *Human Biology* compiled by a group of Oxford professors a curious regular pattern becomes clearly defined. Out of forty scientifically identified Neanderthal men, only one was over fifty years of age; out of 76 representatives of the Paleolithic Period, only two reached that age. The average lifespan in Ancient Egypt calculated on the basis of research on mummies was 22 years; in the Middle Ages it did not exceed 30 years. In the middle of the 19th century this index in Europe amounted to 38 years, and by the beginning of our century it increased to nearly 50 years. From 1900 to 1950, the population of the United States over 60 years of age increased by 274 per cent. In France the number of old people doubled within one hundred years.

According to the data of various demographers reported at the 9th International Congress of Gerontologists held in Kiev, more than 15 per cent of the people living in Europe are sixty years or older. In the whole world there are 280 million people in this age bracket.

In one of his last works Professor B. Urlanis published the following estimates: if we consider that the world population today is not more than 5 per cent of all the people that were ever born, then the number of people over 70 years of age who are still alive is approximately a third of all the old people that ever lived.

Professor A.M. Merkov, a Soviet demographer and medical statistician, has traced the change in the average lifespan in Russia and the USSR over different thirty year intervals:

1896-1897—32 years;
1926-1927—44 years;
1958-1959—69 years.

At present, the average lifespan in the Soviet Union, just as in the United States and on the European continent is holding at approximately 70 years. According to the predictions of demographers, by the year 2000, it will rise to 73.9 years in the developed world.

Tuberculosis and severe infectious diseases are losing ground to other factors as the primary causes of mortality. In the first decade of the 20th century, for every 100 000 people of the population, 200 died from infectious diseases in Spain and Denmark, and approximately 100 to 150 died in Britain, Belgium, Germany, Italy, the United States and Japan. In the seventies, these figures in the economically developed capitalist countries ranged from an average of 4.2 people in the Netherlands to 22.1 in Austria per 100 000 of the population.

Success was achieved by protection of the sources of water, extermination of disease-carrying insects, widespread vaccination of the population, and treatment with antibiotics.

The older generation is gradually forgetting, while the younger generation has only heard of such diseases as typhus, the plague, cholera and smallpox, aptly described by A.I. Herzen as diseases that were "native" to Russia.

Having reached the stage of "greying hair", people today no longer die from old age as a rule (the biological lifespan is longer than the usual lifespan by nearly 20 years), but from several diseases typical for their age, among which cardiovascular diseases rank first and cancer second.

According to data released by the Central Statistical Board of the USSR, in 1978 it was precisely these diseases that were responsible for 65 per cent of all deaths—51 per cent and 14 per cent, respectively. According to data from the World Health Organization, the same proportion is typical of all developed countries, where cancer claims from 13 to 24 per cent of all deaths.

Statistical comparisons for the years 1900 and 1965-66 reveal that cancer death rates, per 100 000 of the population, have increased: from 84 to 225 persons in England and Wales, from 59 to 234 in Belgium, from 66 to 153 in the USA, from 52 to 162 in Italy, and so forth. In Japan, the rate of increase in cancer deaths outpaces similar indices regarding cardiovascular diseases.

What has caused the increased number of cancer patients? Certainly, an important factor is that diseases are now more accurately diagnosed and recorded. The main reason, however, is the change in the age distribution of the population towards a greater number of the elderly and old. Thus, we are justified in saying that it is not cancer that is spreading, but rather more people are reaching the age vulnerable to cancer.

This is why the problem of preventing malignant new growths has grown so formidable in the latter half of the 20th century. It is not only one of the most aggravating but, quite probably, the most complicated of medical problems. It comprises a multitude of components: the biological understanding of the nature of cancer, the early detection in patients, the diversity of methods of treatment. Any one of these components constitutes an intricate task to solve.

Let us examine the social aspects of cancer. Regarding tuberculosis, it was easily recognized that social factors played a major role in the incidence of the disease: starvation, and crowded unsanitary living conditions were clearly known as factors promoting the spread of this disease. This was known long before Koch discovered the bacillus, and the joint offensive launched against poverty and the infectious agent yielded excellent results. Either component alone, the social or the biological factor, would never have ensured the elimination of tuberculosis as a ubiguitous disease.

Cancer, certainly, is a social evil since it places second in claiming deaths, but it has proved to be very hard to establish the direct dependence of its origin upon the living conditions of the population.

The epidemiology of cancer is a science which appeared not so long ago. Scientists hoped that by studying various geographic locales and different ethnic groups they would manage to reveal those peculiarities which, although they did not cause the disease, might at least promote its development. They succeeded in discovering a great number of interesting facts.

It was found, for example, that some forms of cancer can be linked with the patient's diet, with some harmful habits, with the saline composition of the water that one regularly drinks, etc. At the same time there were contradictions which eluded explanation. For example, there is an ethnic group the members of which invariably drink water which contains a low concentration of magnesium salts: the incidence of carcinoma of the stomach in this group is statistically higher than in others. Not all persons in this group, however, fall ill. To be more precise, in general very few people fall ill, because cancer, itself, is a rare disease. If, on the average, carcinoma of the stomach occurs in 30 out of 100 000 people, in this group we observe that the number rises to 45. For some reason the remaining 99 955 people are not stricken. Consequently, it follows that those 45 individuals suffered from carcinoma of the stomach caused by other factors in addition to drinking water of inferior quality.

We have cited only one of the innumerable paradoxes of oncology. It is as if this disease escapes epidemiological or sociological analysis.

The same may be said about experimental research and other problematic questions. This does not mean, as some people are inclined to think, that we know nothing at all about cancer and can do nothing about its prevention. Whatever is already known and what remains a mystery, what disappointments we have experienced and what hopes we now have is the subject of the ensuing chapters of this book.

Facts and Reflections

What is What?

Before even trying to formulate any provisos, we would like to remind you of what Alexander Pushkin, that poet of genius, once said: "Define the meaning of your words and you will rid people of a good half of their delusions."

What is cancer? It would seem there is no simpler question that one could pose to an oncologist. Nonetheless, it is just as difficult to find an answer to this question as to explain the meaning of the concepts "life", "health" and "disease".

In encyclopaedic dictionaries a disease is defined as an impairment of the vital activities of an organism resulting from functional or morphological changes.

Very often, however, anatomical aberrations may only be variants of the normal condition depriving man neither of his ability to live, nor of his ability to work. Short stature, for instance, is most often the result of genetic factors and a man who is not tall may easily be quite healthy, strong and talented. A height of less than 150 cm, on the other hand, is a most important, at times the only symptom of hypophysial nanism, a disease which may be successfully cured if a growth hormone is administered at an early age (before the skeleton has completely formed).

As yet the "material basis" for many diseases has not been found. These diseases, however, can lead to severe conditions, to the loss of working capacity. They can prevent a person from being an equal and fully functioning member of the society he lives in. This mainly concerns some types of mental disease.

But may a person be considered healthy after undergoing a serious operation?

In patients with gastric or duodenal ulcer, sometimes part of the stomach is removed when necessary. This operation has saved tens of thousands of people from agonizing pain, and even from death, but, in a few of the patients operated on, their digestive function was damaged in some way: sometimes this was evidenced by short spells of dizziness and weakness after meals, but at times the consequences were far worse. And a new term appeared in the medical literature—disease of operated stomach.

Who can rightly be considered recovered after surgical intervention and who must still be regarded as ill? Various criteria, both clinical and laboratory in substance, have been applied. The results of tests which determine how well food is being digested were taken into consideration. As a consequence of this analysis, former ulcer patients were unjustly categorized as ill.

N.N. Petrov, an eminent Soviet surgeon and oncologist to whom we will refer many more times in this book, has clearly defined his approach to this problem. He does not believe in looking for a disease on the basis of its laboratory indications: in his view, a person must be considered healthy if he behaves like a healthy person, i.e., he does not complain and he performs the same work he did prior to the operation.

This approach is supported by the fact that in Russian the word "disease" (bolezn') stems from the word "pain" (bol') which signifies a pathological condition of a living being.

Academician Nikolai Amosov, the well-known surgeon and writer, asserts in one of his books *Reflections on Health* that it is practically impossible to draw a dividing line between two seemingly opposite concepts—health and disease. Avicenna, who lived more than a thousand years ago, was inclined to think the same; between these two poles he distinguished various transitional stages.

Thomas More once wrote that health is joy itself or inevitably gives rise to joy, just as fire creates warmth. With due respect for the English philosopher it would be hard to agree with his dictum because it is far too naive. This idea probably came to him after recovery from illness: one begins to value health more keenly when there is danger of losing it.

The French social-hygienist Dubos, who wrote *Mirage of Health*, claims that health is the state of man's complete adaptation to his habitation. Accordingly, by improving the conditions of life, equilibrium may be attained at a lower level of health. During recovery after myocardial infarction, a person will feel healthy if he observes a prescribed regimen and limits his activity. It is not without reason that Karl Marx once described disease as life limited in its freedom.

Academician I.V. Davydovsky, an eminent theoretician in medicine, came to the following conclusion: "Disease is life, a form of the organism's adaptation to the conditions of existence."

It thus proceeds from the above that there is no clear-cut division between health and disease, because both one and the other are manifestations of life.

What about cancer? What difficulties are there in defining cancer?

Approximately 200 years have passed since the Lyons Academy announced a contest for the best answer to the question, "What is cancer?" Bernard Peyrilhe was the winner with the reply: "Cancer is a disease which is just as difficult to define as it is to cure." (Incidentally, at the present time the International Agency for Research on Cancer is in Lyons.)

The complexity of defining cancer consists primarily in the fact that the term covers approximately 200 malignant diseases. Cancer is merely the generic designation for a variety of processes, just as in the last century the term "fever" referred to a large number of diseases attended by high body temperature and chills.

Since one of the main outward distinguishing signs of cancer is the presence of a tumour (plus tissue), we must first clarify this concept.

Tumours are generally differentiated by two characteristics: their origin (i.e., the tissue in which they appear), and the way they develop and grow.

Regarding the first sign, tumours may be classified as epithelial (they derive from epithelial tissue such as skin, mucosa, etc.), and as connective tissue tumours (which arise from connective tissue such as bones, tendons, etc.) The latter also include tumours of the lymphatic and haemopoietic systems.

Epithelial tumours are called carcinomas; connective tissue tumours are called sarcomas.

Tumours may be malignant or benign. The latter do not "spread" in the body and, as a rule, cause no discomfort to the patient; however, in certain localizations (the brain, for example) they may cause even tragic consequences.

The differences in principle between the first and second are shown in the following table.

Benign tumours	Malignant tumours
Usually slow growth	Usually rapid growth
They move the tissues apart as they grow	They grow destroying surrounding tissues into which they penetrate deeply
No metastases	Frequent metastases
The structure of the initial tissue is preserved	Structure of initial tissue substantially changes
Cells multiply at the same rate as in healthy tissue	There are many dividing cells

The unit structure of the tumour is the cell.

When the Dutchman Leeuwenhoek first identified a cell through a microscope in 1673, its structure seemed extremely simple: there were just three components, namely, the nucleus, protoplasm and cell wall. Gradually, the illusion of simplicity faded away, but awareness of the fine mechanisms in the cell continues to this day.

The protoplasm contains mitochondria, which are responsible for cell respiration, and lysosomes, which are tiny formations containing very active enzymes. It is most probable that the latter also protect the cell from harm. Each cell is separated from its neighbour by a membrane. Nonetheless, the live and healthy organism is by no means a colony of individual cells independent of one another, nor are the membranes fences between them. Contacts between the cells which make up a single whole organism are accomplished through these biologically "sensitive" membranes.

All the future diversity of the cells is programmed in the chromosomes found in the nucleus of the ovule (which has been fertilized by the spermatozoon). In the last decades the chromosomes have been shown to consist of unique structures of deoxyribonucleic acid (DNA).

It is generally accepted that progress advances along a spiral. We cannot resist adding that in this case the rapid development of biology and medicine in our time advanced along a "double spiral", just as two threads wound tightly around each other build the DNA molecule, the principal hereditary substance. These DNA threads are a combination of four nucleotides (adenine, guanine, cytosine and thymine) joined by residues of phosphoric acid. The two chains of nucleotides are joined by hydrogen bonds: between adenine and thymine, and between guanine and cytosine.

The structure of deoxyribonucleic acid (DNA) was discovered by James Watson, an American, and Francis Crick and Maurice Wilkins, two Englishmen. This discovery was one of the greatest scientific events of the 20th century.

Every cell contains a reserve of hereditary information in its nucleus. At different stages of embryonal development and throughout the cell's life only specific genes are used for creating the cell's form and fulfilling its function.

In response to "instructions" or "orders" given by the spiral DNA molecules, some cells become the cells of internal secretion glands and produce the appropriate hormones, while others may behave as hepatic cells (and none other), producing only hepatic cells when dividing, and so forth. Thus, the cells are all strictly differentiated, both morphologically and functionally.

The number of cells in an organism is stipulated by the demands of the organism. It has been established to date that there are special mechanisms which are capable of regulating the growth of cells and of inhibiting their unbalanced multiplication. If part of a rat's liver is removed, the remaining lobes continue to grow until the organ attains its initial size. If, for some reason, the cells "escape" control, surplus tissue forms.

It is important to note that the "unplanned" surplus of cells does not alone indicate cancer or a malignant tumour. Tissue proliferation also occurs in benign tumours. Malignant growth is pathological, an extreme variant of cell reproduction.

In contrast to normal cells, which may multiply fifty times on the average in a lifetime, cancerous cells are capable of multiplying endlessly and they can hereditarily transmit this ominous "ability to their multitude of successors". A paradoxical situation is thus created: the "immortality" of the cell is paid for by the death of the organism.

For a better understanding of this process just imagine that in an anthill, where the duties of every ant are strictly specified and where every single ant stubbornly labours for the common good, idle freaks begin to appear which only eat and reproduce. Since they reproduce faster than normal ants, they gradually begin to crowd out the industrious insects, penetrating other sections of the anthill, altimately disorganizing its structure and functions.

The malignant neoplasm grows long and secretly. It can be compared to an iceberg, the invisible underwater part of which is 7-8 times larger than the visible part. The tumour produces no visible clinical manifestations for years and causes no distress, but, once it has attained a certain "critical mass", it begins to develop more rapidly and in a much shorter period of time than that of the symptomless period of growth. The further development of the tumour is manifested by metastases: the flow of lymph and blood transport the tumour cells, they settle in new parts of the body and give rise to secondary daughter foci of the disease.

It should be noted that the pathological reproduction of cells is not the only example of a natural biological process which seems to have grown wild and kills the human being. The same is at times true of the process of inflammation. The "mighty protector" of the organism, which prevents the penetration of various substances of alien origin, primarily of pathogenic microbes, fairly often turns into a merciless enemy. Millions of people have died from purulent infection, pneumonia, osteomyelitis and similar diseases.

Cancer is, therefore, not a "mysterious killer" as it had been considered until quite recently. The nature of cancer is to a great extent known. It is based on sufficiently comprehensible disorders of normal development which readily yield to study and analysis, making it possible to control them even now and, to a certain measure, prevent their development.

Plus Growth, Minus Differentiation

It is very difficult to study human cancer: the patient must be saved and not simply used as an object of scientific research. Moreover, until very recently physicians practically could not observe the early stages of the disease, and clarifying the causes of its origin, by studying neglected forms, held no promise.

It was necessary to experiment on animals. Let us recall that the impressive discoveries made by the "microbe hunters" also became possible only due to laboratory experimentation.

The research offensive against infectious diseases was conducted in the following way: First, the microbe was isolated from the patient and a "pure" culture was grown. This was used to infect experimental animals. The microbe now isolated from the diseased animals was identical in properties with the microbe taken from man. This was a brilliant experimental outline to follow because it provided assurance that the true cause of the given infectious disease had been found and that the appropriate counter-measures would be applied. It is true, however, that not everything went smoothly all the time. When it was necessary to identify the causative agent of leprosy, it thwarted every attempt to transplant into an animal. This is precisely why it took so long to control leprosy as compared to other diseases.

The triumph scored by microbiologists inspired the fighters against cancer. Attempts were made to transplant tumours from man to laboratory animals. Dozens of researchers began working with enthusiasm, but for several years there were no results. Finally, in 1876, at the suggestion of the Russian physician M.M. Rudnev, M.A. Novinsky, who was working on his dissertation in the Veterinary Department of the St. Petersburg Medico-Surgical Academy, successfully grafted the tumour of a dog to a puppy of the same breed. This work marked the beginning of experimental oncology.

Despite the significance of Novinsky's accomplishment, transplanted tumours are not quite the same as those which grow spontaneously in a human being and, in particular, they are unsuitable for researching the causes of cancer. It became obvious that the problems regarding the etiology of cancer could only be solved if we could learn how to induce cancerous tumours in healthy animals.

It had been known, as we mentioned earlier, that skin cancer frequently occurred in chimney-sweeps whose clothes were impregnated with coal resins. In 1889, the German scientist Hanau rubbed this resin into the skin of rats. He did this every day for many months but with no results. The experiment was finally abandoned. Twenty five years later, however, the Japanese scientists Yamagiwa and Ichikawa proved to be more successful. They were aided by (in their own words) "untiring patience" and a lucky choice of animal model for their experiment—a rabbit's ear. Science was thus provided with an opportunity to witness artificially created cancer.

A curious change of sequence took place in later years. Formerly, experimental oncology followed the development of general biology and the same experiments taken from general biology were repeated on tumour material. Later, however, the methods and objectives of experimental oncology became the research subject of general biology and the great diversity of oncological research began enriching biological science.

When thinking about the nature of cancer, people very often confuse two questions, namely, what is cancer and why does it originate? Unless these concepts are taken separately, it is easy to get lost in a maze of theories and suppositions.

Most malignant neoplasms are of clonic origin, in other words, the cellular elements making up the tumour derive from one single cell.

Before a healthy cell transforms into a tumour cell it obviously undergoes a long series of changes acquiring properties substantially different from what there had been at the start. It is practically impossible to trace all these stages because the lifespan of a normal cell is limited and its period of replication (division) may coincide with the period of tumoral transformation. In this case the cell itself will not yet be malignant, but the progeny of succeeding generations, although not of the first generation, will be. Despite these difficulties there are nonetheless models, both experimental and clinical, which permit one to see the principal stages of this process.

In the forties, the American scientist Papanicolaou reported that he had actually diagnosed the disease by microscopy of smears (which contained only a few single cells) taken from the surface of a tumour. His report was questioned by the most eminent histologists, who argued vehemently that a tumour is recognised by the diversity and position of its cells. It took many years of effort for Papanicolaou's followers (among them was the Soviet professor N.N. Schiller-Volkova and the school she headed) to establish the competence of making a diagnosis by studying the structure of different cells. Today one cannot even imagine an oncologist working without the application of cytological diagnostics.

The method brilliantly proved its value during prophylactic examinations of women. Studies examining scrapings from the neck of the uterus (an absolutely harmless procedure) have already yielded both medical and social results, saving thousands of lives. Moreover, oncologists have been given a chance to observe the cells from the very first stages of disorder in their structure through the appearance of definite signs of the primary forms of malignant tumours. In rare instances, when female patients rejected treatment, real developed cancer could be identified.

These stage-by-stage observations can be compared with the scenes of stages of construction as viewed from the window of a moving train: along one section of the way a foundation pit is being dug, along the next section the foundation is being laid, then the walls are erected, and soon the new building is ready and its tenants are moving in with their furniture. The flashing of these small pictures, of course, does not correspond to the strict order of housing construction. One patient may reveal cancerous cells that have already been formed, while another patient may demonstrate various stages of change in cellular structure. Thus, in the jigsaw puzzle of facts gathered, scientists were able to recreate, in principle, the process of tumoral transformation, supporting the clinical material with the results of experimental research.

Can a clear-cut borderline be drawn between rapidly reproducing proliferating cells and cancer? If it can, where does it cross?

Professor V.S. Shapot, a Soviet experimenting oncologist, thinks that this borderline occurs at the moment when morphological and biochemical changeability is manifested in the dividing cells. It is precisely at this moment that the natural selection of cellular elements takes place, i.e., of the more autonomous ones, those which grow more rapidly, resistant to the defensive reactions of the organism, and better adapted to a sparse supply of oxygen. The formation of a malignant tumour is actually testimony that natural selection paves the way for the individual development of a multicellular organism.

As we mentioned before, tumour cells lose their structural and functional differentiation as they mature. They become independent of the control and signals of the whole organism and of the tissue they are developing in. A sufficiently illustrative example of such autonomy is the enlarging tumour found in a starving man, when all the normal cells are atrophied.

The complex of cancerous cells is built more primitively than the tissue of origin. This phenomenon is called anaplasia. Thus, for instance, the transformed anaplastic cells of a tumour of the mucosa at times completely lose their normal ability to secrete mucus; the tumour of muscle tissue loses its contractive ability, and so on. Cell anaplasia develops to such a degree, that it becomes extremely difficult, sometimes impossible, to determine, even with a microscope, from which tissue the tumour has originated. Even the principal function of the living cell, which is to produce protein specific for the given tissue, changes. In some tumours "a return to the past" is observed, and they begin synthesizing protein characteristic of the embryonic period of development.

The central question of the preceding chapter was "what is cancer" and now, in summing up what has been said, an answer may be offered. The shortest and most comprehensive definition of a malignant tumour belongs to Academician L.M. Shabad. It consists of two words and two arithmetical signs: " + (plus) growth, — (minus) differentiation".

Kept Under Suspicion

Since the tumour cell reproduces tumour cells and not healthy cells, the obvious conclusion that can be drawn is that the very essence of transformation is connected to genetic aberrations. This point of view conforms to certain facts.

By electron microscopy researchers have noted differences in the outward appearance and number of chromosomes. In some malignant diseases of the blood an additional chromosome was discovered (known as the Philadelphia chromosome). Nonetheless, this is not a universal feature, because in many tumours the chromosomes are "untouched".

According to the mutation theory of the German scientist Bauer, unfavourable external influences give rise to radical changes (mutations) in the genes controlling growth. This theory seemed to be well corroborated in experiments producing hybrids. More thorough experiments were carried out in which melanomas were induced in swordfish hybrids.

In Central America, there are two species of fish which are closely related: the pecilia and the swordfish. The pecilia has visible black spots on its dorsal fin, which contain the pigment melanin. The first generation hybrid of the pecilia and the swordfish demonstrates more of these spots along with a considerable number of neighbouring areas covered with red spots. Another crossbreeding of the hybrid with a "pure" swordfish yields progeny which have extensive patches of melanin soon after birth; in addition, practically the whole body turns red. Within a few weeks, pigmentary tumours (melanomas) develop from these patches and the fish perish. These tumours, which were exclusively genetically induced, are considered truly malignant, because they can be grafted to fish of the same species, they metastasize, and they possess several other characteristic signs.

The above experiment provided convincing proof of the important role of mutation in carcinogenesis, but further experiments on plants and on a model typical for geneticists, the Drosophila fly, showed that the mutation of genes and the appearance of tumours often do not coincide. There are many agents which cause mutation but are incapable of inducing cancer and, vice versa, if the tumorigenic activity of a substance were evaluated by its ability to cause mutation, then many doubtlessly carcinogenic substances would have been labelled inactive. This means that mutations can occur without the formation of tumours and cancer can be induced without firmly established mutation.

Clinical observations and the latest experiments allow for a completely different evaluation of the "genetic laboratory" of tumours.

A study by doctor S.N. Nasipov, for instance, examined the incidence of esophageal carcinoma by looking into the genealogy of such patients living in the Guryev Region. He found that in 116 out of 254 cases both husband and wife became ill with the disease. This provided evidence that the cause stemmed not so much from genetic predisposition as from the existence of other common factors which had affected the family.

It is evident to all that the role of heredity is particularly obvious in twins. In one of his works, however, Professor V.P. Efroimson cites the following data: out of 375 pairs of uniovular twins, of whom at least one member died from cancer, the corresponding death of the second twin was registered in only 12 per cent of the pairs. In other words, the fact that the inherited genotype was identical was not of decisive importance in this case.

On the other hand, according to data collected by epidemiologists, the blood relatives of patients with congenital developmental diseases of the organs suffer a higher incidence of malignant neoplasms than a control group of people. Similarly, the risk of breast cancer is increased by several tens of times in females whose mothers or sisters had suffered from the disease. Both cases, however, can be explained as being caused by the action of some type of carcinogenic agents during the intrauterine period and as by no means due to the disturbance in the genetic code of the sex cell. It is also quite probable that the inherited predisposition to malignant tumours plays a role, but only under certain conditions. In this case, conducting investigations which will identify these conditions and their elimination will help to remove the threat.

In recent years it has been convincingly demonstrated that the genetic code of the cancerous cell is not "broken" but is actually identical to the genetic code of the normal cell.

Until the middle of the 20th century the ovule (more precisely, its nucleus) was believed to be the only carrier of all hereditary information. Then, Gurdon at the Oxford University performed an experiment demonstrating that the nucleus of a frog intestinal epithelial cell contains the complete set of genes necessary for the future organism in all its diversity. By a complex microsurgical procedure, the scientist removed the nucleus from the ovicell of the frog and replaced it with the nucleus from the intestinal epithelial cell. The ovicell developed into an ordinary tadpole and eventually into a normal frog.

The British scientist R.K. MacKinsey removed the nuclei of frog ovicells and replaced them with the nuclei from tumour cells. Just as in the experiments of Gurdon, viable tadpoles resulted, providing evidence that the nuclei of tumour cells retain the complete information for the entire series of specialized cells.

These experiments, however, failed to resolve all the existing doubts because the tumour, from which the nuclei had been removed, had been induced by a virus and during transplantation the virus may have been lost while the genetic material was left whole. Moreover, the tadpoles did not develop into frogs, thus leaving much unclear.

A new experiment was required, preferably on mammals, but for a long time this was unattainable.

One day, however, the journal of the New York Academy of Science reported on success achieved by the American geneticist B. Mintz. She had chosen mice for her experiments. The initial genetic material used were the cell nuclei of a very dangerous (ascitic) tumour which Dr. Stevens reinoculated in new mice specimens every 2-3 weeks over the duration of eight years.

In the experiment, the "ascitic tumour" was induced by introducing malignant cells into the abdominal cavity of a mouse, where they caused the accumulation of fluid (ascites), thus creating a natural thermostat for themselves. The cells of this tumour, which were injected subcutaneously in mice, invariably gave rise to malignant neoplasms, which rapidly, in a matter of 3-4 weeks, killed their "host". The carriers of the tumour were black male mice.

After this the nuclei of cancerous cells were used to fertilize the blastocytes (embryonal nodes) of a white mouse and these were then implanted into the uterus of another white mouse. Healthy young mice were born; some of them had a mosaic pattern of coloring typical of white and black mice. The further mating of a mosaic male and female led to the birth of a small black mouse. It possessed the complete hereditary set of its black mice ancestors.

This provided proof that the nucleus of the tumour cell contains all the genetic information necessary for the normal development of the animal. Thus follows the correct assertion that in malignant transformation the genetic code is not broken, i.e., mutation does not occur.

This does not mean that changes in the hereditary apparatus of the cell never play a role in carcinogenesis. Questions concerning heredity are extremely complicated. It is quite probable that the key to this problem lies in the "repression" of genes, in the exclusion of part of the genetic code from activity and the stimulation of other parts responsible, in particular, for the rates of growth and reproduction of the cell.

Reflecting on the work of B. Mintz, two important conclusions may be reached:

First of all, tumoral transformation of the cell is, in principle, reversible.

Secondly, the tumour cell is not "alien" to the organism.

The latter phenomenon may possibly explain the difficulties encountered in the early detection of cancer and the failure of all attempts at active immunization, which are based on the search for specific markers distinguishing tumour from normal cells. This information may upset our conceptions of the nature of malignancy. A vast perspective is opened up for research which is currently being carried on throughout the world.

The following story illustrates how difficult it is to properly estimate the significance of genetic factors and their relationship with other factors of carcinogenesis.

During the first postwar years no serious discussion concerning the origin of tumours ever took place without heated clashes of opinion. Our generation of young physicians at that time specially attended such meetings in order to hear the debates of two brilliant scholars and polemicists: Lev Shabad, who championed the hypothesis of carcinogenic substances, and the virologist Lev Silber. Since "Lev" means "Lion" in Russian, among ourselves we dubbed these discussions "the battles of the lions". With equal erudition and mastery, basing their arguments on firmly established experiments, both eminent scientists presented their seemingly completely incompatible points of view. Time, however, proved them both to be right.

These debates contributed to the development of our ability to think scientifically; they demonstrated how difficult it is to make correct judgements. We again realized the genius of Hippocrates' foresight, for he once said that experience is fugacious whereas judgement is hard to make.

In short, the matter came to the following: by selective cross-breeding according to the rules of genetics researchers succeeded in producing a "high-tumour" strain of mice, in which carcinoma of the mammary gland often occurs spontaneously in females, and a "low-tumour" strain, in which it is encountered very rarely. The experiments were extremely labour-consuming; for example, in order to obtain "pure strains", Maud Slye in Chicago expended several million mice.

The genetic "basis" for breast cancer in mice was not questioned, but suddenly in 1936 the American virologist J. Bittner presented new evidence, when female newborns of the "high-tumour" strain were taken from their mothers, and fed by mice of a "low-tumour" strain, the percentage of tumours appearing in the mice when fully grown was 16 times less. Conversely, if a female of the "high-tumour" strain feeds mice of the opposite strain, these mice (when mature) demonstrate an increased incidence of cancer. It follows that a certain "milk factor" must exist and cancer of the breast in mice is not genetically predetermined.

Further immunological research and electron microscopy established that the "milk factor" is a virus, but its origin and effect are closely related to the natural functioning of the organisms and their tissues, and is conditioned by them. The "milk factor" was found only in specific genetic strains of mice. In mice of other strains lacking this virus, cancer of the breast may be induced by carcinogenic substances which are devoid of the "milk factor". A virus exists in males of the "high-tumour" strain, but normally it does not cause cancer; however, the introduction of female sex hormones in these males induces cancer. The connection of the "milk factor" to the specific genetic profile and the stability of the internal medium of the organism is obvious.

It should be emphasized that we are discussing only certain populations of mice: the "milk factor" has not been detected in other animals and in man.

What can be concluded? There is no doubt that the nucleus, containing the substratum of heredity, is involved in transforming a healthy cell into a tumour cell. At the same time it is becoming more obvious that the "genetic programme" does not play the decisive role in carcinogenesis, because it is far from effectual in some instances: there is a definitely clear division between hereditary processes and the development of the tumour cell.

What Failed?

Researchers also began to suspect lysosomes. These are minute organelles containing various enzymes capable of splitting proteins. Injury to the cell is followed by the release of these biologically active substances which destroy the cell: the cell appears to "commit suicide". During inflammatory processes when the organism must quickly do away with "spoiled" cells, the lysosomes perform the duties of a "sanitary brigade". In the scientific literature of the last decade it has been speculated that the lysosomes seize and possibly destroy undesirable external agents that penetrate the tissues, such as polycyclic hydrocarbons and dyes. This fact may be of importance in changing the biology of the cell and in tumoral transformation.

Another important element is the mitochondria, which are responsible for cell respiration. Several respiratory enzymes are concentrated in them. In essence, nutritive substances are metabolized, evolving oxygen and hydrogen which under the action of enzymes enter into reactions, producing energy and water. Some authors have aptly referred to mitochondria as the "power plants" of the cell.

Another form of respiration, however, is also possible, namely, glycolysis, i.e., glucose is decomposed without the uptake of oxygen from the environment, resulting in the formation of lactic acid. According to the observations of Professor V.M. Zykov, one of the founders of Russian oncology, and the German biochemist O.H. Warburg, this so-called anaerobic type of metabolism proved to be characteristic of the tumour cell. In the thirties Warburg demonstrated by simple experiments that the microscopic sections of a tumour absorb less oxygen and produce more lactic acid than healthy tissues.

The conception prevailed that any carcinogenic influence first affects the mitochondria. Warburg contented that carcinogenesis induced by X-rays is none other than the disruption of respiration due to the death of mitochondria. He cleverly defended his thesis on the role of glycolysis, basing it on the generally accepted opinion that tumoral transformation of a cell is simply a return to the primitive state.

"We know from geology that before oxygen appeared in the atmosphere there were some forms of life on Earth. These were undifferentiated unicellular organisms which lived without oxygen, but were capable of glycolysis. It was only when free oxygen appeared in the atmosphere (which occurred about 800 million years ago), that all of a sudden life began to develop rapidly and the plant and animal kingdoms were formed. Thus, evolution is the result of the activity of oxygen, or, to be more precise, of oxygen respiration. The reverse of the process of differentiation of highly developed somatic cells is today most vividly manifested in the development of cancer."

Warburg further formulated his theory most conclusively: tumour cells develop from normal somatic cells in two stages. Just as the appearance of the plague is conditioned by the sum total of seemingly unrelated factors (heat, the presence of pests and rats) although caused by the plague bacillus, the development of cancer is linked to a large number of factors. Some of these factors are coal resin, radiation, arsenic, a low partial pressure of oxygen in the cells, urethan, and sand; however, the immediate cause to which all these factors lead is the irreversible disruption of cell respiration. This is followed by the second stage in the development of cancer—a long struggle by the damaged cell for survival, a struggle in which some of the cells perish due to lack of energy, while others manage to make up for their energy losses in cell respiration at the expense of energy obtained through glycolysis. However, because of the morphological inferiority of glycolytic energy the highly developed somatic cells become dedifferentiated chaotically growing cells, i.e., cancerous tumour cells.

This is how the eminent German scientist, author of what seemed to be a convincing theory of carcinogenesis, evaluated the importance of just one cellular organelle.

Unfortunately, this theory, just as many others, was not universal, although there were instances of its brilliant practical application for the prophylaxis and treatment of the disease. For example, there is a form of carcinoma of the larynx and esophagus occurring in Scandinavia, which is easily detected in its early stage. If medical agents that intensify the effect of respiratory enzymes and compensate for their deficit are infused in patients with early signs of the disease, the patients are completely cured without any additional treatment.

What prevented Warburg's theory from being recognized as universal? It was established that far from all malignant tumours rely on anaerobic respiration. At the same time high glycolytic activity is also observed during inflammation and tissue regeneration. Moreover, it would be wrong to consider the respiration of the cell or tissue isolated from other types of metabolism, because they are closely interconnected in the organism. Finally, the most important objection is that neither Warburg nor his followers ever proved that the disruption of cell respiration was the primary factor, and transformation of the healthy cell into a tumour cell, the secondary factor. What if anaerobic glycolysis is characteristic of an already anaplastic, transformed cell? In this case it is not the cause, but the result.

Here, one cannot keep from drawing an analogy: when the ships of Christopher Columbus sailed into the Caribbean and the sailor perched on the mast shouted, "I see land", neither Columbus himself nor his companions had any doubt that they had reached India. Columbus believed in this illusion to the end of his life. Actually, at that historic moment he had not even reached a continent but had discovered a comparatively small island. Several dozen years elapsed before the contours of a vast continent and many islands to the east of America took shape.

Similar things have happened in the science of oncology. In 1923, when Warburg discovered anaerobic glycolysis in tumorous tissue, he was certain that he had found the only correct approach to cancer, to which he devoted over 30 years of his life. In actual fact he had only revealed one of the characteristics of the tumour cell.

Since we have touched upon the subject of metabolic processes, however, it is appropriate to discuss the contribution made by biochemistry in uncovering the secrets of carcinogenesis.

Beginning with the first investigations by the Russian oncologists V.M. Zykov, D.V. Nenyukov, M.N. Tsukerman, and V.A. Bogorodsky in 1911, biochemical research in this field never stopped. The answer to the problem was more than tempting: if it were possible to find a metabolic feature exclusively characteristic of malignant tumours, then biochemical tests could easily diagnose patients in the early stages of the disease and treatments based on Warburg's method (as mentioned above) would reassure that the golden age of cancer prevention had arrived.

Researchers of the laboratory headed by Professor V.S. Shapot established that malignant tumours act as a peculiar trap for glucose which is pumped from arterial blood as into a vacuum (an expression coined by Shapot). A whole cascade of disorders in the metabolism and function of the internal secretory glands results. The decreased content of sugar in the blood leads to inhibition of the insular apparatus of the pancreas which in the long run decreases the assimilation of glucose by peripheral tissues. This is compensated for by the increased utilization of fatty acids as an additional source of energy.

This or that metabolic derangement of the patient's organism, however, effects a quantitative rather than essential changes. After many years of hard work and intensive study of the international scientific literature, Shapot came to the irrefutable conclusion that there are no biochemical reactions or processes in malignant tumours which do not take place in normal cells and tissues.

How is this possible? On the one hand, tumour cells behave differently from healthy ones and are capable, in the long run, of killing a person. On the other hand, there are no essential differences between these cells. How can this contradiction be explained? Perhaps the problem will become clearer if we consider the brilliant comparison offered by our most eminent authority in experimental oncology, Academician L.M. Shabad. Imagine three strips of cloth: red, white and blue. If we arrange them lengthwise in a certain pattern, they form the state flag of the Netherlands. If we place them at right angles to the first pattern, they form the state flag of France. And if we fold the blue strip into a corner, while the remaining two run lengthwise, we have the national flag of Czechoslovakia. The countries mentioned are absolutely different, as are their flags, but three colours suffice to express the symbolism, though even the quality of the strips may be the same. The distinction lies in precisely the way the strips are laid out. Could there be a better illustration of the case where the same quantitative composition but a different combination or arrangement of elements produces such dissimilar results?

Another structural component of the cell participating in carcinogenesis is the cell wall, the membrane. A separate isolated cell exists only in microscopic sections (not counting primitive unicellular organisms); in real life billions of cell communities exist in mutual interdependence and intercommunication. Some researchers even speak of "cell sociology". The communication between cells, which is expressed by their exchange of vital materials, by their correct location in the system of the given tissue, and by growth or inhibition, is expressed via membranes.

Tumour cells differ from healthy cells mainly by their unrestrained proliferation, and this feature, as had been mentioned, is to a large measure due to the loss of communication with the organism.

Metastasis is a no less important characteristic. Schematically this takes place in the following manner: cells or cell complexes of the tumour break away from the tissue of origin, penetrate into the spaces between tissues, and enter the lymphatic or blood circulation systems where they are carried away to the nearest lymph nodes and eventually to remote organs where they begin living as daughter tumours (metastases).

This ability to metastasize and seize surrounding tissues (infiltrative, invasive growth) is made possible by the specific characteristics of cell membranes. These became known after researchers learned to grow tissues outside the organism in a special nutrient medium. It was demonstrated that tumour cells are more easily separated from one another than normal cells. Surface membranes have a comparatively higher negative charge and even repulse each other according to Coulomb's law. Moreover, the degree of malignancy of the cells and their velocity in an electrical field are directly linked: the more malignant the tumour, the more independent are its cells.

In studying the behaviour of cells in different organs both in the intact organism and outside of it, researchers discovered certain patterns which can only be explained by the properties of biological membranes.

For example, if the cells of healthy tissues are grown in a nutrient medium, while dividing and developing they move freely until they encounter others like themselves. On meeting, their further migration is halted. Scientists called this phenomenon "contact inhibition". It may be illustrated by a witty quotation from Schopenhauer: one fine winter morning a family of hedgehogs gathered together to warm themselves at their neighbour's expense. However, they began to feel the needles of their neighbours sooner than the warmth, and the company split up and each went his own way. When, in their search for warmth they nevertheless from time to time attempted to gather together, they always encountered the needles of their neighbours. Finally, choosing the lesser of two evils, the hedgehogs preferred to keep at a reasonable distance from one another.

A malignant tumour presents quite another case. Here, the cells cannot perceive their neighbour's proximity and continue to multiply, forming large chaotic accumulations. Their behaviour in a sick animal is no different from that in tissue culture, which experimenting oncologists in the Federal Republic of Germany (R. Süss *et al.*) very aptly described as "antisocial".

The "ability" of cells in healthy tissues and organs to build specific structures is truly remarkable. If the cells of different species of animals are mixed together, they group into clearly divided complexes. In another experiment, suspensions were prepared with kidney and liver cells from experimental animals; a mixture of both suspensions was grown as a single culture in a glass vessel containing a nutrient medium. Observations revealed that on finding one another the cells of the liver began forming their own organ on a miniature scale. The cells of the kidney "behaved" in like manner. Tumour cells were completely lacking in this ability.

It appears that disrupted membrane functioning is the reason for unrestrained growth, infiltration of the surrounding tissues and metastasis; however, another stipulation must be made. Changes in the membranes cannot be specified as the one and only cause of carcinogenesis; in fact, absolutely healthy and normal blood cells (granulocytes, lymphocytes and others) lose their connections to neighbouring cells as they mature and circulate alone without the slightest sign of malignancy. Evidently, we are dealing with yet another manifestation of the tumoral transformation of cells.

Let us return to the question we posed earlier: How can we be sure that damage of cellular membranes is the cause and not the consequence? Scientists seem to be oriented as to what is going on, while the main question of science, Why does this happen?, remains unanswered for the time being.

The combination of all the above-described deviations in the biology of the tumour cell sometimes produces a clear picture which pathologists use in making a diagnosis.

What are the signs that the doctor seeks as he looks through the microscope? First and foremost he is checking the polymorphism of the cells. In ordinary tissue the cells are practically identical in shape and size; in malignant tumours two absolutely identical specimens are rarely to be found. The nuclei of cancerous cells are often brightly coloured and not in their strictly allotted place, but in any "sector" of the cellular area. At times one can see not just one, but two or more nuclei of different size.

In these cells substances identifiable by special dyes and characteristic of the initial tissue (for example, mucus) may be absent and new components may have formed which are not normally present ("corneal pearls", etc.). In healthy tissues some cells are usually observed at different stages of division (mitosis); in a malignant tumour there are many more of these cells and very often they are of obvious pathological character.

The combination of these signs along with others of importance to specialists makes it possible to assume the existence of a malignant tumour even if only single cells are examined under the microscope.

While looking through the limiting eyepiece of a microscope at these cancerous cells cut off from the surrounding world and concentrated on a tiny area, one finds oneself captivated by the diverse, turbulently dividing sea of elements with blue-eyed nucleoli and one forgets that they herald death.

The diagnosis is made more precise if the behaviour of the cells in the tissue is evident. In cancerous tissue the cells are positioned chaotically as if tumbling over each other, violating the tissue strata, invading neighbouring structures. As was mentioned, it is at times impossible, even with a microscope to determine how the tumour cells originated and what they replaced. In such cases it is said that the tumour is anaplastic, that it has lost all the properties of normal tissue.

But again we come up against a familiar paradox: Electron microscopic studies under the supervision of Academician N.A. Krayevsky revealed remnants of differentiation that had survived anaplasia, and in some cases showed no specific morphological signs of malignancy at all. It is striking that these data are in complete agreement with the conclusions reached by Shapot, which were mentioned above: no substances or processes occur in a tumour cell that are not encountered in normal cells.

The opinion of scientists regarding the absence, in principle, of biochemical and morphological distinctions between a tumour cell and a healthy cell is reminiscent of a curious story told by an eminent biologist. This biologist was once invited to the laboratory of a colleague, who specialized in the field of electron microscopy. It is well known that this method can magnify objects by tens of thousands of times in order to study structures invisible through a conventional microscope. After a tour of the laboratory and a scientific discussion, host and guest lunched while continuing their conversation. They obviously liked each other and it was then that the biologist was shown the latest equipment of great resolving power. On becoming acquainted with the "superpowerful" electronograms that had been produced the biologist thought: "This man of genius is departing infinitely from the truth!"

We by no means believe that the microworld should not be further explored. After all, there is no limit to knowledge! But in order to understand the malignant cell it is probably more important to discover those quantitative distinctions which when summed up reveal new properties connected with anaplasia, the loss of differentiation with all its consequences. Nor does this contradict the daily practice of pathologists: when they study the tumour through a microscope they can make a precise diagnosis.

At the same time intensive research at the cellular level leads us to think that the tumour cell originates from a normal cell and becomes sick as a result of protracted changes. There is an even more important conclusion, although purely theoretical as yet: the tumoral process is, in principle, reversible.

In the USSR many eminent oncologists have investigated reverse development. Academician A.S. Serebrov, basing his research on experiments performed by V.A. Parnes and I.A. Rappoport, presumed that the tumoral process can be interrupted at any stage, and that this could be accomplished by paralyzing the antienzymatic effect of the tumour virus and reestablishing control over division. V.Ya. Shevlyagin contends that if the origin of the tumoral transformation of the cell is the insertion of the genetic material of the virus into the cell genome, it would be fairly reasonable to presume that the complete removal of the detrimental genetic information of the virus would be attended by the reverse transformation of the cell into a healthy one.

Elaborating on the research of N.N. Petrov, Academician R.E. Kavetsky pointed out that even before all the linking factors of carcinogenesis are revealed it will be necessary to find ways to affect its separate mechanisms with specific agents or conditions in order to prevent tumour development. Kavetsky perceived of several theoretical possibilities to accomplish this task. Schematically they are reduced to the following:

(1) replace the "damaged" RNA in the leukaemic cell with corresponding whole RNA;

(2) synthesize the "normal" gene by fine manipulations, and introduce it into the malignant cell to return the cell's initial properties;

(3) stimulate the differentiation of cells;

(4) treat with hormones and enzymes to normalize the interaction of cells;

(5) study the possibility of using the cell's own defensive forces, in particular, interferon;

(6) find the "levers" necessary for the reestablishment and maintenance of immunosurveillance.

An extensive programme was thus proposed. Kavetsky was sure that by blocking the linking stages of carcinogenesis it would be possible not only to cause the death of tumour cells, but to reduce the degree of malignancy and intensify their differentiation. He based his proposal on the theory of the reversibility of cancerous cells. The seemingly fantastic nature of this programme should not discourage the reader as a great many ideas in modern science at first appeared improbable but later yielded real and positive results.

A Dangerous Encirclement

The first part of our narrative focussed mainly on those processes which are inherent in the tumour cell; now we shall try to explain why they originate.

A multitude of theories exist and it would be difficult and even unnecessary to delve into all of them. There are two theories that command the greatest interest today. One theory suggests that cancer develops as a result of external chemical influences; the other theory states that it is of viral origin. It must be mentioned that the possible appearance of malignant tumours under the influence of external (exogenic) physical factors such as traumas and radiation lesions has been proven.

Cases where cancer or a sarcoma has developed at the site of traumatic injury are comparatively rare. L.M. Shabad carefully investigated this possibility and quoted N.I. Pirogov's apt statement, that "war is a traumatic epidemic". If trauma were truly a major cause of cancer, we could expect every big war to be followed by an "outbreak" of tumours, primarily, sarcomas of the bones and soft tissues of the limbs. It is well known, however, that no increase in the incidence of such diseases has occurred although over forty years have elapsed since the Great Patriotic War. This general observation is not changed by individual cases linking the appearance of cancer with a trauma. Each case has its own explanation.

Of course, oncologists have dealt with patients who explain that their tumour (most often situated externally) had been preceded by a mechanical injury; however, it can usually be proven that a potentially malignant tumour had been injured which accelerated the development and intensified the clinical picture of the disease.

Radiation lesions present quite another case. Here, the carcinogenic role of the external influence leaves no room for doubt.

The description of the first "X-ray carcinoma" in man has been published and republished in successive medical texts ever since it occurred in 1902. A German technician who checked X-ray equipment used his own hand as a control. He exposed his hand to radiation and judging from the X-ray produced he regulated the emission and determined the serviceability of the tube. The result was tragic. At first the technician suffered from severe dermatitis, skin ulcers followed, and ultimately he developed cancer of the skin.

In 1936 a monument was erected on the square of the Hamburg Roentgen Institute in honour of the commemorating 169 scientists, engineers and physicians who fell victim to the hazards of experimenting with X-rays. In 1959 the Memorial Ledger already contained 360 names, including 13 of our Soviet compatriots.

Frederic Joliot-Curie attempted to analyze the radioactivity of his parents' manuscripts by using a counter hooked up to a loudspeaker. He detected signals of the radium his parents had extracted nearly 60 years before.

Pierre and Marie Curie's fingerprints contaminated with radium had been left on the pages of their diaries. The pioneers in this research naturally had no idea how risky their work was and took no precautionary measures. (Marie Curie's contemporaries testified that 15-20 years after they had begun such investigations, there were considerable traces of radiation injury on the skin of her thumb and index finger.)

Descriptions of the effects of radiation on women who worked at a small factory in New Jersey during World War One painting instrument dials with luminescent paint containing radium and mesothorium have become a common textbook example. At that time this production process was new and nobody suspected its insidious effects. The women received piece-rate pay and soon found it more efficient to lick the brush first to bring its hairs to a point and then dip it into the paint. They naturally ingested tiny amounts of the radioactive mixture in the process. Ten to fifteen years later bone tumours were found in several dozen women. Why?

When radium enters the organism it behaves like calcium; that is, it penetrates the bone and settles there. In contrast to calcium, however, it destroys osseous tissue. Changes occur which gradually lead to the development of a malignant tumour. A threat also mounts for the white blood corpuscles which are produced by the bone marrow: exposure to radioactive radiation may induce leukosis. Large doses cause death because of anaemia and haemorrhages within a few years; the effect of smaller doses is evident in 20-25 years, generally in the form of malignant tumours.

A special medical discipline soon arose called radiation hygiene, which develops and applies safety measures for preventing radiation lesions.

Scientists began experimenting on animals and succeeded in producing a great variety of tumours depending on the radioactive material they had on hand, its dose, the number of exposures to radiation and the intervals between exposures, the way the radioactive agent was introduced, and the biological peculiarities of the mammals experimented on. The carcinogenic effect of ionizing radiation was established for certain, but did this satisfy the oncologists?

First of all, radiation energy is a rather rare cause of tumoral transformation. Second, the absolute, or, as it is termed, the linear, dependence between the irradiation dose and tumour development was not established. It is probable that it is not the hereditary apparatus of the cell which is directly affected, but its metabolism, and tumoral transformation is a secondary development. The most interesting observations were the changes in hormonal balance due to irradiation, resulting in the proliferation of tissues in the organs under hormonal attack. This eventually leads to malignant new formations. In spite of the controversy still existing, the study of radiation carcinogenesis yields invaluable information on the causes of cancer and on how to prevent certain forms of this disease.

One of the first attempts to provide a scientific explanation for the origin of tumours dates back to 1775 when the

English doctor Percivall Pott (mentioned above) described cancer in chimney-sweeps caused by soot.

It was in England again that attention was focussed on the workers repairing roads who frequently handled resins, bitumen and asphalt. These men suffered from skin cancer at a rate four times higher than the general population. A higher incidence of cancer is also correlated with other occupations: workers in the gas industry, non-ferrous metallurgy and asbestos factories are more vulnerable to lung cancer; bladder cancer is more common among workers in the aniline industry.

Let us examine another case such as that of arsenic. Farmworkers, who spray vineyards with arsenic-based insecticides, have a higher rate of carcinoma of the liver. Tumorous lesions of the skin have long been known to result after prolonged treatment with arsenic-containing drugs. Many cases of cancer have been documented among people who regularly ingested water from artesian wells which had a high content of arsenic.

Here we are confronted with another paradox of which there are an abundance in the science of oncology. Arsenic obviously has a carcinogenic effect on humans, but a similar effect cannot be produced in experimental animals.

Nevertheless, it is now perfectly clear that long-term contact with certain chemical elements actually promotes the development of malignant tumours.

This fact presented new problems for scientists to solve: in the first place, the substances which possess carcinogenic properties have to be identified in order to establish prophylactic procedures and safety standards. Further, experiments using animal models present the opportunity to uncover the patterns governing the transformation of the healthy cell into a tumour cell. Finally, it must be understood why carcinogenic substances affect only a small proportion of the people with whom they come in contact.

The plague, cholera, influenza and other infections are far more simple to deal with than cancer. Science has at least discovered their causative agents which affect practically everyone that happens to be in the focus of the epidemic.

John Snow, an English doctor who lived in the middle of the 19th century, gave the following description of events which occurred in London in 1854.

A few weeks ago, on Broad Street, on Golden Square and in adjoining districts the worst outbreak of cholera in the history of the Empire occurred. On a stretch of about 250 metres where Cambridge Street joins Broad Street, up to 500 fatal cases were registered in just ten days. The mortality in this limited area was obviously no less than at the time of the plague, but seemed all the more striking, because in most cases the patients died in a matter of hours. If the inhabitants of the neighbourhood had not fled the district, the mortality would have been even higher... On evaluating the situation and locating the focus of the spreading epidemic, Snow began to suspect that contaminated water that local residents had been taking from a street water fountain in Broad Street was responsible for the outbreak... More than 60 people testified that those who had fallen ill had used the water from Broad Street regularly or from time to time... In the evening of September 7 Dr. Snow met with members of the St. Jacob Church Council and told them what he had surmised; the following day the handle of the fountain was removed. After this the cholera epidemic began to abate.

Oncologists can still only dream of eliminating external chemical carcinogens (or, at least, of reducing the number of deaths caused by cancer) as easily as Snow had identified and removed the source of the cholera outbreak. Unfortunately, this is far from simple.

In the Soviet Union Academician L.M. Shabad and his pupils devoted many long years to study the factors that are conducive to the development of cancer. Their work revealed that carcinogenic substances may be present in polluted air, water, and living quarters. Thus, the prophylaxis of malignant tumours is closely linked to the problem of environmental protection.

The modern inhabitant of Earth is often compared to a special kind of centaur who is half human and half machine, whose gasoline breath pollutes the air. Airplane pilots testify that over any large American city clouds of brown fumes can be seen at a distance of dozens of kilometres. In their travel notes around the United States, correspondents V. Peskov and B. Strelnikov compare the air above enormous residential blocks to the vapours of a chemical brew and write that driving through some city streets is like groping through a smokestack.

The air above Moscow today is cleaner than that of any foreign city of the same size. This is to a great measure due to the fact that Moscow is one of the greenest capitals in the world. In Paris and its suburbs there are six square metres of vegetation per inhabitant, 7.5 in London, 8.6 in New York and 18.5 in Moscow. The planting of greenery is promoted in all Soviet urban communities.

Trees are not merely the "lungs" of concrete cities. From a report published in the newspaper *Pravda*, interesting research conducted by Professor S.V. Durmashidze revealed that some species of trees, such as fir, for example, are capable of extracting carcinogenic substances from the soil (even such active chemicals as benzopyrene and nitroso compounds), and decompose and use them for their own metabolic processes. Thus, prospects for making the environment healthier have also opened up at this "biological" level.

Scientists are interested in the mechanisms of action of carcinogenic substances, their source of origin, the ways for rendering them harmless, their turnover cycle in nature, etc. Large-scale state-organized protective and planning measures are based on this research, in particular, the rational planning of urban communities, regulating the functioning of plants and factories, controlling the disposal of wastes into the water and atmosphere. Technologies are being improved to prevent the pollution of water and air, and industry is promoting closed cycles in using air and water.

Shabad and his colleagues have demonstrated that smaller amounts of carcinogens and shorter periods of contact with them postpone possible sickness with cancer and reduce the number of patients ill with the disease. Shabad's hypothesis formulated about twenty years ago provides hope that mankind can be protected from the harmful effect of external factors and also provides a real basis for state institutions and public organizations to undertake large-scale measures for the prevention of cancer. It is not accidental that Article 18 of the Constitution of the USSR reads as follows: "In the interests of the present and future

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generations, the necessary steps are taken in the USSR to protect and make scientific, rational use of the land, its mineral and water resources, and the plant and animal kingdoms, to preserve the purity of air and water, ensure reproduction of natural wealth and improve the human environment."

An important and timely law has been passed establishing state regulation (inspections in various fields) over the daily implementation of measures aimed at environmental protection. The problems involved in making the human environment healthier are currently being tackled on an international scale.

According to one opinion, the dinosaurs which vanished from the face of the Earth 65 million years ago perished from food poisoning. It was precisely at that time that gymnospermous (naked-seed) plants, which were the food of those gigantic animals, were replaced by the higher flowering plants which contained many alkaloids. The dinosaurs never succeeded in adapting to these new "chemical additives". This is something to think about.

The avalanche of new compounds which have appeared in the 20th century must be scrupulously tested. We must learn to determine which of them possess direct or indirect toxic effects and exclude them from use.

At first the list of carcinogenic substances grew very rapidly. First on this list were components of black coal resin (anthracenes and petroleum derivatives); then followed a group of metals including nickel, beryllium, chromium, lead, zinc, copper and cobalt. Later, turpentine, orange, eucalyptus and croton oils were added.

Bearing in mind the possibility of occupational cancer, dyes were tested for carcinogenicity, and it was demonstrated that the intermediate products of dye production (aromatic amines) induced the appearance of tumours in experimental animals.

We are in full agreement with the American researchers Raven and Roe who contend that there are infinite ways that food is contaminated by chemical carcinogens. Food may be contaminated by synthetic packaging materials, the inner surface of tin cans, and labels printed with printer's ink. "Accidental" contamination may occur in the storehouse or during transportation. Moreover, some foodstuffs at times inherently contain carcinogens.

At the beginning of the sixties simultaneous observations were made in Britain and the USA which, at first glance, did not appear directly related to oncology. Up to 69 per cent of the turkeys grown in several English counties perished within a short period of time causing a serious blow to farming. Not only scientists but even Scotland Yard was called on to investigate the situation. It turned out that the young fowl had been raised on caloric Brazilian peanuts, or rather, the flour made from such nuts. This was not the first year however, that such fodder had been used. Where was the answer to this riddle?

At the same time, in the United States, fishermen became very alarmed by an "epidemic" of cancer of the liver (hepatoma) in trout. Moreover, it was noted that fish raised artificially in breeding ponds suffered most, whereas "wild" trout caught by fishermen were quite healthy.

It was not long before scientists decided to compare the increase in the rate of hepatoma with the transition from liquid to dry feed. Cottonseed was found to be the culprit.

Scrupulous laboratory analyses, however, revealed that the peanuts and cottonseed were not responsible for the death of the fish and fowl. The diseases had been caused by a substance produced by the mold that attacked foodstuffs of vegetable origin during their storage. Based on the Latin name of this mildew, the substance was called aphlatoxin. It has not been established as yet whether aphlatoxin plays any role in human carcinoma of the liver, although scientists are inclined to link the high incidence of carcinoma of the liver among Negroes of the Bantu tribe with the fact that their diet consists mainly of wheat or maize. If one takes into account the climate in which the Bantus live and store their grain (great heat and moisture), it is highly probable that they constantly ingest aphlatoxins with their food.

The increased incidence of lung cancer in most economically developed countries is to a great extent caused by air pollution. It is not surprising that this form of cancer is not typical of rural inhabitants. Air pollution is particularly harmful under certain weather conditions, when smoke particles are suspended in fog, creating smog—a moist cloud which blankets a city for hours on end. Could this be the reason why foggy England, where smog is an all-too-common feature, leads in mortality due to lung cancer?

Women breathe the same air as men, but they succumb to lung cancer six times less frequently than men. Apparently, the problem is not so simple and a second factor, such as smoking, evidently plays a part. (The proportion of females among lung cancer patients is currently growing. This is the price they pay, as Professor A.V. Chaklin, the well-known Soviet onco-epidemiologist, aptly put it, for their outward show of independence,—the cigarette.)

It is precisely the combination of life and work in the polluted atmosphere of a big city, plus smoking, that paves the shortest way to contracting lung cancer.

In essence, it is the smokers who are the subjects of a great oncological experiment. R. Süss and coworkers have very convincing evidence: in the United States, approximately a million people were under observation for over eight years. Mortality due to lung cancer among smokers proved to be ten times higher than among non-smokers. As for particularly avid smokers, matters are even worse. Those who consume two packs of cigarettes a day increase their chances of joining the ranks of oncological patients by 24 times.

A survey in Britain yielded similar results. Those who smoke 25 or more cigarettes a day die from lung cancer twenty times more frequently. Men from 50 to 69 years of age who have never smoked fall ill 17 times less frequently than those who smoke 20 cigarettes daily. And those who gave up smoking from 1 to 10 years ago have a 2.5 times lower rate of illness than men who continue smoking a pack a day.

Such statistics caused one epidemiologist to exclaim: “Only ignorance or bias can explain why some people deny the existence of a real connection between smoking and contracting lung cancer!”

Up to 90 per cent of the combustion products of tobacco remain on the bronchial mucosa in smokers. The majority of carcinogenic substances collect in the cigarette-holder and, therefore, it is inadvisable to smoke a cigarette down to the butt. The efficacy of tobacco filters, which at first seemed to guarantee “safe” smoking, proved to be very low, just as the once-advertised “harmless” cigarette.

In the 1960s, R. Doll, an eminent English oncoepidemiologist, once wrote, the advertising of cigarette smoking is one of the most notable absurdities of our age. In 1970s, the Executive Committee of the International Union Against Cancer adopted a decision to appeal to all governments to pass a law restricting the advertisement of tobacco. A few years later the Executive Committee reiterated its appeal.

Such advertising has been banned in most countries at this time, and a warning is printed on cigarette packages to the effect that smoking is detrimental to one's health. For many years a systematic anti-smoking campaign has been carried out in the Soviet Union by the press, radio and television. Since the first step towards becoming a smoker is usually made when one is quite young, the responsibility naturally rests first and foremost on the family and the school. If, for instance, both parents are smokers, their children frequently also begin to smoke—44 per cent of the sons and 37 per cent of the daughters. If they wish to protect their offspring from this, the parents must first break the habit themselves and create an atmosphere of intolerance to smoking in the home.

The pernicious habit of smoking is akin to another traditions widespread in the Orient and the Southeast that often leads to severe consequences, namely, the habit of chewing betel or nas. The latter is a mixture of tobacco, ashes, lime and oil. Many people addicted to chewing nas eventually develop carcinoma of the oral cavity which originates precisely at the spot where the mixture is habitually placed. In different regions different ways of using nas have developed: some addicts shove it under the tongue, others, behind the right or left cheek. Accordingly, the carcinoma originates at either one of these sites.

Several years ago at a symposium of Soviet and Polish oncologists, Polish physicians presented an interesting case. A high rate of carcinoma of the stomach had been registered in one of Poland's rural areas. Specialists investigated the traditions of food preparation in the given locality and found that housewives usually cook their food with melted pig fat that has been reheated and remelted over the course of a week or more. When the lard is heated to high temperatures over and over again in the cast iron pan, it changes in chemical structure producing substances which, when continuously ingested with food, give rise to cancer. In experiments on mice, scrapings from the frying pans behaved like typical carcinogens. This research provided concrete material for developing prophylactic approaches to cancer.

Nutrition evidently plays a substantial role in the development of cancer. Professor N. Dungal from Reykjavik studied cancer morbidity in Iceland and found a correlation between the appearance of a tumour and the length of time that smoked meat and fish were used in the diet of the population.

The advocates of the theory of carcinogenic substances consider a strong argument in their favour to be the well-known fact that under natural conditions tumours usually develop from the epithelium (the upper layer) of the organs bordering between the external and internal media such as the skin, gastrointestinal tract and lung. The epithelium of these organs fulfills a barrier function and is the first to encounter various harmful substances.

Carcinogenic substances have a harmful effect not only through a direct "encounter" with a human being, but also via the organism of the mother—intrauterinely—on the maturing fetus.

The discovery of this mechanism was to some extent due to an accidental meeting which again confirms the primary importance of contact between scientists in different fields of research. In an oncological institute, in the USA, an elevator once broke down. The scientists were obliged to ride another elevator located at the opposite end of their building near the laboratories of the morphologists. As a result, the researchers often casually exchanged opinions on professional subjects. Once, one of the morphologists happened to mention that within a short period of time he had come across two cases of a rare tumour, specifically, light-cellular carcinoma of the vagina. Soon afterwards he mentioned that he had again made such an observation, thus arousing the professional interest of his colleagues who responded by conducting a scrupulous oncoepidemiological investigation. They revealed that light-cellular adenocarcinoma of the vagina is more frequently encountered in young girls and women who were born to mothers whose pregnancy had been maintained by means of intensive courses of treatment with methylstilbestrol.

Later, a special international register was established for tumours whose origin is linked to the effect of different factors during pregnancy. To date several hundred such descriptions have been entered in the record. Moreover, Japanese scientists have convincingly proved that undesirable "interventions" during pregnancy are fraught with the hazard of tumours that may develop not only in the next generation, but even two generations later.

The problem of transplacental carcinogenesis developed into one of the most urgent issues of modern clinical oncology and anti-cancer measures. In the USSR, this research is headed by N.P. Napalkov, Academician of the Academy of Medical Sciences, at the Petrov Oncology Institute in Leningrad. Incidentally, as far back as 1926, Nikolai Petrov himself warned that cancer prevention begins with pregnancy hygiene.

Nevertheless, in discussing the role of carcinogenic substances in the development of malignant tumours, one should not overestimate their significance. The American writer B. Glemser stated his opinion on the subject quite figuratively, asserting that it would be more correct to say that only a few people manage to survive miraculously in this carcinogenic ocean. He explained that when one starts to think of the factors causing this malignant disease, one gets the impression that there is only one way to avoid cancer: one must stop breathing (because polluted air may be carcinogenic), stop eating (because traces of carcinogens have been found in food), never step outside one's flat (because there are viruses which, as may be eventually proved, are actually the primary cause of all these things), and so on.

One could easily add to this list and suggest disposing of all medicines (a report was published in 1974 stating that reserpin may cause cancer), cosmetics, and discontinuing the use of water; in other words, to eliminate everything that surrounds us and sustains life.

Endogenic factors of carcinogenesis may also be added to this list. It is truly remarkable, but carcinogens are constantly present in the organism of animals or man and under certain, as yet not clearly defined conditions, they may suddenly become active.

Already at the turn of the century physicians noted that deviations in the functioning of the sex hormones are in some way connected with the appearance of cancer of the breast. Later, experimental evidence convinced them that various hormonal influences induced both non-malignant and malignant tumours of the breast, uterus, sex glands, thyroid gland, bones, hypophysis, and so on, in experimental animals. Just like chemical carcinogens, hormones do not induce tumours in all animals. Evidently, the initial constitution, the condition of the liver, the peculiarities of metabolism, etc. are important factors. Finally, active carcinogens had been produced by the liver in animals who had died from cancer of other organs.

It looks like we are "under siege" by the enemy from within and without; however cancer is not at all such a frequent disease. Many people do not suffer from malignant tumours although they live in the same "sea of carcinogens".

There is a strong basis for presuming that the decisive role in the development of cancer is played by a disorder of the internal medium of an organism. This reminds one of an episode from the history of microbiology.

In the latter half of the 19th century, when the question of the nature of infectious diseases was considered far from solved, the leader of Koch's ardent opponents was the 73-year-old scholar and physician specializing in hygiene, Max Pettenkofer. He refused to believe that the vibrio discovered by Koch was the causative agent of cholera. The American writer Paul de Kruif reproduced his method of proof as follows:

When Koch's absolutely precise experiments failed to convince old Professor Pettenkofer from Munich, the latter wrote to Koch requesting him to send some of the vibrios so that he could prove that they were harmless. On returning from India, Koch sent him a test tube filled with the most "vicious" culture of cholera vibrios. To the horror of all the "microbe hunters" Pettenkofer, on receipt, immediately swallowed the contents of the tube which contained enough vibrios to kill a regiment of soldiers. He smoothed his beard and said: "Now let us see whether or not I become sick with cholera!"

By some absolute miracle he did not fall ill...

Pettenkofer, however, who had irrationally performed such an act, proved to be sufficiently intelligent to link the results of his experiment with the problems of predisposition.

"Embryos play no role in spreading cholera," he declared. "The crux of the matter lies in individual predisposition."

"There can be no cholera without choleric vibrio," countered Koch.

"But I swallowed several million of your fatal bacilli," remonstrated old Pettenkofer, "and I did not even vomit!"

Alas! As often happens during fierce scientific controversies, both sides were simultaneously right and wrong.

Nevertheless, why is it that every contact with a carcinogen does not necessarily give rise to disease? Why do malignant tumours occur mainly in elderly people? (Statisticians have found that the incidence of cancer increases with age at a rate of 2^5 to 2^6.) Could there be a connection here? Perhaps carcinogenic factors have a long term of action.

Long ago, Hippocrates, in his treatise on diet, warned that the factors causing disease do not have an immediate effect. They ripen gradually and manifest themselves only later. The longer a human being lives, the more harmful influences he experiences. Genetic errors accumulate in the process of ageing; however, as mentioned above, mutagenic and carcinogenic influences do not always run parallel. At the same time there are usually signs of intensive ageing in the patient's organism, even if malignant tumours develop at a young age. The well-known Soviet endocrinologist and oncologist Professor V.M. Dilman pointed out a similarity between the metabolic peculiarities inherent in normal ageing and the changes caused by chemical carcinogens. Primarily there is insufficient utilization of glucose and prevalent use of fatty acids as a source of energy. The surplus of cholesterol, triglycerides, certain lipoproteins and insulin that naturally occurs in the process promotes the division of both normal and tumour cells, disturbing the functioning of cellular immunity.

These circumstances make it possible to regard ageing as a leading factor in carcinogenesis, or, to apply V. Dilman's term, "one of the ten 'normal diseases' linked with ageing". (According to Dilman, obesity, diabetes mellitus in obese people, atherosclerosis, hypertension, metabolic immunodepression and several other diseases are included in this group.)

Obesity is of great interest to us, because with an increase in body weight, the probability of tumour development increases. There is convincing data that the simple reduction in food calories makes it possible to delay the development of malignant tumours in experimental animals.

It has long been known that stout individuals live a shorter life than thin people, but, as wits hasten to add "they get more fun out of life". Whereas the saying, "while the fat man dries, the thin man dies", is not confirmed. According to statistics, corpulent individuals are 1.5 times less likely to live to seventy years of age and 3 times less likely to reach eighty. In this case the "biological clock" runs faster than a person's chronological age.

A persons's constitution to a large extent reflects the metabolism of the organism. According to numerous investigations carried out by Soviet and other scientists, females with a pyknic type of body build have a higher incidence of breast cancer and sex organs. This is taken into account in forming the so-called "high-risk groups" which are subject to constant medical observation and thorough prophylactic examinations.

The goal of science lies not only in acquiring knowledge but also in benefitting the health of humankind. The normalization of metabolism must serve as that control lever which, although it may not totally prevent cancer, at least delays its development even before we thoroughly understand all its undisclosed mechanisms.

Filterable Agents

Our discussion about the possible causes of the development of malignant tumours would be incomplete if we did not deal with the role of viruses—minute beings which occupy a mysterious place between living and inanimate nature. Their indeterminate status is due to the fact that although they possess a hereditary apparatus represented by one of the nucleic acids (DNA or RNA) and a protein membrane, they multiply by a method of reproduction different from all other living organisms. Lacking their own "building materials", viruses can grow and multiply only inside the living cells which they parasitize. They do not multiply by division but by a set program that intracellularly directs the synthesis of their separate components, which are then assembled to form new viruses.

The first speculations that cancer may be connected to viral infection date back to the turn of this century when the lucky "microbe hunters" were replaced by "virus hunters".

It is true, that at that time no one (or practically no one) gave serious thought to the statements made by the French microbiologist Borrel (1903) and the outstanding Russian biologist I.I. Mechnikov (1909) regarding the possible viral origin of cancer. Even the investigations by the Danish scientists V. Ellerman and O. Bang and the American P. Rous (1908-1911), who infused a non-cellular tumour filtrate into experimental animals managing to "infect" them, passed unnoticed.

Such neglect can only be explained by the fact that, first of all, all this was too similar to the stage which had already passed namely, the rejection of the infectious theory of cancer, and second, chemical carcinogens were on a triumphal march. Moreover, the extreme methodological difficulties in handling viruses had delayed the further accumulation of facts by more than 20 years. It was only in 1933 that the American scientist R. Shope discovered the virus of rabbit polyoma, and three years later, J. Bittner produced the so-called "milk factor", which was discussed above.

L.A. SILBER

Scholars were reminded of all this in 1946 when the book by L.A. Silber, *The Viral Theory of the Origin of Malignant Tumours*, was published in a small paperback edition. No serious work in the field of the theory of oncology comes out today in which the authors do not directly or indirectly refer to the ideas of the late

Academician Lev Aleksandrovich Silber. This is not only because he was a brilliant scholar and a distinguished polemicist, whose interests reached far beyond the already extensive field of questions that he studied, but because he was also a generous scientist freely sharing his ideas, many of which are being successfully developed today by entire schools of scientific thought.

Lev Silber was born in 1894; his father was a musician. The whole family was unusually gifted. Silber himself had a fine ear for music, he was extremely well-educated, knew several languages fluently and could speak about almost any complex subject making it easily understandable for any of his listeners. His written works are literary models of a very high quality.

Silber was the prototype for several heroes in books written by his brother, the famous writer V.A. Kaverin.

An aura of brilliance attended everything Silber spoke about or did, and it fitted splendidly with his desire to achieve prominence or at least become noticed. His friends jokingly called him a "hussar", and, to be sure, there was much of the hussar's cocky spirit in Silber, in his love of life, which characterized all his statements, actions and decisions. He was tall, lean and handsome, a tireless wit and gallant in his attentions to women. At the same time he was an eminent medical theoretician.

One of the authors of this book was fortunate to have had the opportunity to know him, to attend many of his talks at the peak of his scientific career, and to discuss his own research with him. Even a brief conversation with the scholar gave one the feeling of having been "charged" by a battery. Silber's short critical remarks about our dissertations-in-progress not only provided food for thought about the given material, but threw new light on the general direction of research to be conducted and revealed the meagerness of our post-graduate efforts. It was useless to argue with him, not because of our difference in age or status, but primarily because of his unexpected approach to any subject and the remarkable criteria he judged by. One received the impression that he lived in a separate world of hypotheses and facts that he himself had derived, and that he evaluated the research results presented to him from the position of the scientific and philosophical concepts he adhered to. This was difficult for the still immature young scientist to digest but forced one to look at things from a completely new position.

There are many approaches to scientific research. The simplest and most frequently applied is when a scientist studies some phenomenon step by step, gradually accumulating and generalizing the data obtained. This, for example, is how the great physiologist Ivan Pavlov worked. Having begun by studying the functions of the digestive glands and achieving outstanding results in this field of physiology, Pavlov noted the dependence of the rhythm of saliva production on external factors influencing the experimental animal. Using actually no more than one or two experimental models, he spent the rest of his life collecting, generalizing and explaining data concerning the theory of conditioned reflexes. No wonder Pavlov used to say that data are like air for the scientist.

Silber was another kind of scientists. For him the "air" was the ideas or concept which were formed on the basis of experiment, erudition and free flights of fancy. Later, in specifically planned experiments these ideas were either confirmed or refuted by scrupulously derived facts. Who can say which approach is more productive?

In his book *The Viral Theory of the Origin of Malignant Tumours* Silber cites far more hypotheses than facts and describes experiments performed that produced negative results and could not be explained by theory. It seemed that the viral theory would have to be acknowledged bankrupt. Professor G.I. Abelev, Silber's pupil, wrote that at the time (1945-1947) there were no grounds for confirming the viral theory; on the contrary, there were sufficient reasons to discredit and forget it. To forge a new direction in research is a difficult task, but to launch a new trend in opposition to the generally accepted opinion can only be likened to a scientific exploit.

A head researcher like Silber demands selflessly dedicated colleagues and a special style of teamwork. The atmosphere in his laboratory was aptly described in Kaverin's story *A Two-Hour Walk*:

"...The art of supervising the team rested, in essence, on just two principles...

"The first was frankness and clarity of purpose. Nothing should be done behind anyone's back whether this concerned personal relationships or professional research interests. The reason for the research should be clear to one and all, from the head of the team to every lab assistant.

"The second principle consisted in honesty. An article was very rarely published under one name. It was practically always the result of the combined efforts of two, three, or four authors, and the order in which the names stood was based on the objective evaluation of each of the author's contribution. Favoritism was repudiated and this created an atmosphere of mutual trust."

While retaining the priority of guidelines, directing the research orientation, Lev Silber gave his colleagues a free hand in creative independence and initiative. He was a director without a trace of envy or jealousy regarding the successes of other members of the team.

Before discussing Silber's contribution to science it would be appropriate to describe his personality in greater detail. This is possible because soon after his death his friends and colleagues wrote short recollections about their tutor which are treasured by his family. With the permission of Silber's son the authors of this book have consulted these materials. The main feature of his character which was so striking to everyone who dealt with the academician was his passionate approach to everything. First and foremost was his passion for science that made him fight for his goals and argue with strained nerves. It was precisely this aspect of Silber's character that the late Academician A.I. Serebrov noted in his memoirs. Serebrov was a skilled clinician among Leningrad oncologists who took a great interest in theoretical research. He was a highly educated physician, a charming although stern man, who resembled Silber in the sense that he also believed in fighting against all odds if need be. Silber proved to be correct in many instances even though many of his conclusions at first seemed purely speculative to others. Serebrov writes:

"Silber was unquestionably an eminent scholar who made an indelible imprint in science, particularly in oncology, and one can only envy the passion he displayed in his work and lectures. He was a brilliant polemicist, particularly when the two Levs—

Lev Silber and Lev Shabad—"locked horns" in heated debate over the etiology of tumours.

"I remember that once, after a heated discussion, I drew a caricature of the two lions (Lev means "lion" in Russian) snarling at each other with one saying, "It's viruses," and the other, "No! It's carcinogens!"

Although hot-tempered himself, Silber was tolerant of such character traits in others, and a sharp clash or scientific controversy with an opponent bore no reflection on their further amiable relations.

Many people remember Silber's rapid gait. No one ever saw him shuffling even during the last years of his life. His purposeful drive, reflected in his gait, was one of the peculiarities of this remarkable scientist who, in his research, was ahead of his time. This fiery polemicist, who built theory based on his ideas was, at the same time, very meticulous and consistent in collecting scientific facts. He not only actively participated in running experiments, but took great pleasure in carrying out the preparations for them.

Silber at one time worked as a lab assistant and was skilled in all techniques, such as making emulsions, using a centrifuge, or infusing some agent. His students were often surprised by his serious attitude to elementary technical tasks which, it seemed, he could have easily turned over to others. His meticulousness, however, allowed for no waste of time. He did not overlook a single experimental detail and his scientific conclusions were, therefore, based on facts, leaving no room for doubt. Any artifact, that is, an accidental result not related to the true properties of the research object but due to experimental inaccuracies, was ruled out completely. This is why Silber was always ready to tackle large-scale problems in the shortest possible time. But he was also capable of waiting with great patience.

As an adolescent, Silber struck up a friendship with the future writer Yu. Tynyanov who also lived in Pskov. They went their separate ways and met again nearly ten years later. Kaverin, who witnessed this meeting, later wrote: "...The two young people, Lev was twenty-six, and Yuri was half a year younger, reminisced about their school years in Pskov. How astounded they both would have been if they could have peeped into the future. Many books were to be written about both of them. Yuri was fated to die from multiple sclerosis, a terrible disease which remains mysterious to this day."

It is precisely in connection with his friend's disease that Silber made such a sharp change in his research orientation hoping to restore Tynyanov's health and that of thousands of other people, but sudden tragic circumstances deprived him of the possibility to continue his research for several years, and then it was too late—his friend died. Among the "turmoil" of his new interests, however, Silber did not forget about diseases of the nervous system, and this is where his remarkable "scientific" patience served its purpose; he had the ability to wait for years, if need be, for the desired results.

Professor L.P. Popova, a pupil of Lev Silber, recalls: "The work connected with amiotrophic lateral sclerosis depended a lot on the ability to wait patiently for results. For many long years after monkeys had been infected by extracts taken from humans, no distinct signs were manifested; the disease may have been developing latently. We kept wondering at Silber's attitude to negative results. I remember that once when examining the monkeys, I came across peculiar examples of spontaneous demyelinizing diseases among them. Silber did not ignore these data. On the contrary, the interest that these diseases aroused in clinicians gave new impetus to research. Although at the time Silber was very busy working on tumours, he took part in conferences at our institute on these diseases."

Among clinical neurologists Silber was always an incontestible authority. Even now his ideas regarding the role of slow viruses in the etiology of progressive neurological diseases, such as amiotrophic lateral sclerosis, remain the leading ones.

Last but not least, Silber was always able to win over practicing physicians, arouse their interest and mobilize them for joint scientific endeavours.

Although basically a theoretician, he was invariably involved in finding solutions to the most urgent problems in public health protection. It is not surprising that as far back as the Civil War, he fought against typhus and himself succumbed to the disease twice but recovered and, as he liked to joke, "did not die because of some misunderstanding".

Silber began as a microbiologist and by the years 1922-1923, i.e., at 28 years of age, he had already made a major scientific discovery. He succeeded in proving that it is possible in principle to direct and genetically establish changes in certain important properties of bacteria. Beginning in 1935 he dedicated himself to the study of viruses. He founded the Soviet school of medical virologists and developed this new branch of science.

In the thirties much attention in the USSR was focussed on developing the Soviet Far East. This gigantic national effort was impeded by mass-scale epidemics of encephalitis in the spring and summer. An expedition was sent deep into the taiga in 1937 headed by Silber, who had gained much experience in combatting the plague in Azerbaijan. Within a short period of four months, as a result of the brilliant tactics and selflessness of the director and his assistants, the virus which causes the disease was isolated and its carrier, the tick, was identified. Measures were planned to prevent this terrible disease.

Academician N.N. Blokhin wrote: "This work has long become a classic textbook illustration for organizing investigations of this type; it constitutes the pride and glory of Russian virology."

In 1944 Silber made another sharp turn and first proposed the viral theory of the origin of cancer. His struggle in championing his ideas could serve as the subject of a long dramatic story. Silber spent twenty years proving that he was right and developed his virogenetic concept which now provides the basis for research conducted by many scientific oncological schools.

A new scientific discipline stemmed from the viral theory of the origin of cancer, namely, the immunology of cancer. Not only Silber's immediate students, but many adherents of his theory in different countries of the world devoted themselves to research in this field.

Today there is no longer any doubt that viruses are capable of causing many malignant tumours in experimental animals, including monkeys. From the point of view of oncovirologists, the great variety of tumours known in the animal kingdom can be separated into two groups: these are new-growths, the nature of which has already been or will be demonstrated. It is of interest to note that with every year the category of tumours of viral origin is expanding with the exception of tumours in man, where we can only speak of certain "candidates" of oncological viruses. The primary suspects are the adenoviruses which are found in the tonsils and which cause colds. They induced tumours when introduced in experimental animals, which suggests, but nonetheless still fails to confirm, the viral etiology of tumours in man. Direct evidence may only be obtained "in nature". It should be borne in mind that from the moment the tumour-producing virus is infused to the time the disease is manifest in animals, about one-half to two-thirds of the animal's life has passed. Compare this with the lifetime of man and it becomes obvious how many dozens of years researchers will have to wait, even if they are lucky to find volunteers willing to try out the viral theory on themselves.

The methodological difficulties (and not just these) oblige scientists to look for other approaches to this type of research.

The viral origin of leukemia has been studied for many years at the monkey nursery in Sukhumi under the supervision of Academician B.A. Lapin. There is as yet no convincing evidence that the diseases of man and of the closest animal to him, i.e., the monkey, are identical, just as there is insufficient evidence of the causative role of viruses.

At present the most likely candidate of the oncogenic viruses of man is the filterable agent which gives rise to Burkitt's lymphoma and belongs to the group of herpesviruses (herpes in Greek means lichen). This group also includes the causative agent of "fever blisters" widespread among humans: in this disease the lips become covered with watery blisters which dry and scale off very slowly. Herpetic fever often attends colds.

Burkitt's lymphoma is a disease of the lymphatic apparatus of the neck. The tumour was usually encountered in children from 2 to 14 years of age and, as a rule, it quickly resulted in the death of the child. (We use the past tense because Burkitt's lymphoma can now be cured by drugs in nearly 100 per cent of all cases.)

This disease is named after the British surgeon Dennis Burkitt who worked in Uganda. He discovered this disease at a mature age (about fifty). During his childhood, as a result of an accident, Burkitt lost an eye, but this proved not to hinder his powers of observation and perspicacity. Before Burkitt many physicians had seen rapidly growing tumours which had disfigured and killed African children, but only Burkitt investigated the cause of this disease.

Burkitt polled his colleagues and established that this tumour is not typical for all the regions of Africa. He then decided to map its distribution and did so using the method of his father, an ornithologist, who used to map the regions of the birds he studied. Driving an old Ford, with two assistants, Burkitt went on a safari "hunting the tumour", as he used to say.

The results of this research demonstrated the first malignant tumour in medical history whose "advance and spread" proved to depend on the temperature and humidity of the environmental air. This led to the assumption that the disease was transmitted by mosquitoes, and since these insects are carriers of infectious agents, virologists began their search for the causative agent of lymphoma.

Data gradually accumulated that revealed that the lymphoma described by Burkitt is sometimes encountered by physicians in climatic conditions which exclude the possibility of any carrier. Researchers had to abandon the hypothesis about the role of mosquitoes, but the search switched over to the viruses. The British scientists M. Epstein and E. Barr who isolated this herpesvirus lent their initials to name the culprit EB. Some time later the American scientists Gertrude and Werner Henle established a curious fact: EB proved capable of causing a frequently occurring non-malignant disease of the lymphatic system—infectious mononucleosis.

The first pathologists who studied mononucleosis found it difficult to distinguish from leukemia. In contrast to oncological diseases this disease invariably ends in recovery. Thus, one and the same virus may in some cases induce a malignant tumour, and in others, an infectious disease.

At this point we are obliged to interrupt our narrative very briefly to return to the relationship existing between a virus and an organism.

We have already mentioned that viruses are intracellular parasites. Their progeny develops at the expense of the chemical elements of the cell. Having penetrated the nucleus, the virus introduces its hereditary system into the cell which competes with the more complex hereditary system of the cell itself.

Schematically the duel between the genetic information of the virus and the cell may be represented by three variants. If the virus is in a "commanding position" it begins to reproduce very rapidly and, so to say, explodes the cell from within: this marks the triumph of the viral infection. If the cell proves to be stronger, the virus particles remain without progeny. Finally, the "compromise" variant is the unification of the genetic material of the virus and of the cell. Precisely this integration of two genomes, according to Silber's theory, brings about the malignant transformation.

In observing experimental tumours Silber made known the phenomenon of the disappearance of the carcinogenic virus from the cancerous cell. He presumed that once the virus has ensured changes in the hereditary apparatus of the cell, it can vanish, since in its complete (infectious) form it is no longer required for sustaining the process: at every subsequent division of the cell the "cancer" genes of the virus, which are part of the cell's genome, also multiply and enter the daughter cells.

Silber's virogenetic theory gave a powerful impetus to the development of experimental oncology. This theory, however, had one vulnerable spot: most of the oncogenic viruses of animals contain ribonucleic acid (RNA), whereas the genome of the cell consists of deoxyribonucleic acid (DNA). "Linking" between RNA and DNA is impossible in principle.

This contradiction was eliminated when the American biochemist G. Temin and his colleague S. Mizutani discovered a special enzyme found in virus particles which helped to build DNA on the matrix of the viral RNA. It turned out that it is this newly created DNA which combines with the DNA of the cell.

But far from every "encounter" of the virus with the cell ends either in infection, in the development of a tumour, or in the death of the newcomer. Silber warned that the tumorigenic virus may be in a passive state and that some additional stimulus is required (such as a carcinogenic substance, for example) to activate it.

Further research confirmed that the integration of the hereditary apparatus of the virus with the DNA of the cell is not enough for malignant transformation. There are, at the least, two forms of integration, normal and pathological. Moreover, according to contemporary concepts, first formulated by the famous American biologist Hübner, the viral genome (virogen) is present in all cells. There is even a certain biological sense in this, namely, the virus does not only kill; in order to survive it must be able to co-exist. As a result of thousands of years of evolution, the virogen secured a place in the cells of vertebrates. Biologists with a more extreme point of view contend that the virus in these cells also plays a certain physiological role, but, under the effect of carcinogenic substances, irradiation, or natural ageing, the virogen can actively stimulate the tumoral process.

B.E. Peterson, Corresponding Member of the Academy of Medical Sciences of the USSR, summarized a large amount of data regarding the role of viruses in cell transformation and evaluated them in regard to the possibilities for the prevention of cancer. According to the most recent conceptions about the etiology of malignant tumours, there are different viruses in the cells that are in biological equilibrium with the cell and the organism as a whole and no damage occurs until this balance is disturbed. The cell and the virus are constantly subject to the effect of various factors of the external and internal media: these are exogenous and endogenous chemical or physical blastomogens such as, for example, radiation or ultraviolet rays. Under certain conditions these factors produce an effect, the virus turns aggressive and penetrates the genome of the cell, which leads to several pathological states, to the point when the cell perishes, an oncogenic effect is produced, etc.

It is when the oncogenic effect is produced that new hereditary properties appear as a result of damage to the genetic apparatus of the cell. These properties include continued multiplication, incomplete maturation, and loss of contact with "neighbouring cells". The metabolic processes undergo changes, the cell produces antigens and the organism begins to perceive the cell as a dangerous alien. The immune reaction is activated and, because of the heightened immune responsiveness, the cell that is dangerous to the organism perishes and no tumour arises. This struggle presumably goes on all the time. The older the organism, the more likely that such "confrontations" occur in different organs.

However, if the virus that has been activated in some manner penetrates the genome of the cell, and the cell happens to be in a medium hardly accessible to the immune forces of the organism, or the immune responsiveness itself is weak and incapable of suppressing the threatening reaction at its very start, the cells or group of cells are able to continue multiplying and metastizing unhindered.

On the basis of this concept of carcinogenesis Professor B.E. Peterson has drawn the following conclusion with important implications in medical practice: the only real method for preventing cancer today lies in excluding or weakening the effect of the numerous physical and chemical factors in the external and internal media which intensify the oncogenic action of viruses on the cell.

Can one affirm that cancer is not contagious if some viruses play a "two-sided game", inducing both oncological and classic infectious diseases?

We have been convinced time and again that one factor alone is not sufficient for inducing cancer. Consequently, a virus that can cause the transformation of a cell is not enough; it is necessary that the cell be ready for transformation and that the organism as a whole "misses" this event. And even if viruses are conducive to the development of tumours, they behave differently than in droplet infection (influenza, measles, etc.) There is no question here of contagiousness in the generally accepted meaning of the word. The virus does not "fly" from a sick to a healthy person, but is constantly present in the biosphere of the animal or human organism.

This was not and could not have been known by the Polish physician Clara Fonti at the beginning of the 1950s when she was practicing medicine in Italy. When her husband died of cancer, Fonti decided to devote her life to the struggle against this disease. She was a proponent of the viral theory which was just beginning to win supporters despite stiff resistance. Fonti wished to make her contribution to proving this theory and planned to infect herself directly from a cancer patient.

The history of medicine is marked by the heroic exploits of physicians who attempted by experimenting on themselves to study the pattern of infection and spread of many diseases, to test the safety of new medicinal agents and complicated diagnostic procedures, and to test the reserves of human resistance in a fragile boat among boundless ocean of diseases.

"... Tests performed on oneself are good for novelists, but actually nobody cares much for such beautiful words about cast lots, crossing the Rubicon, and dedicating one's life to science. It is only the natural desire of the researcher to get a tangible grip on the process in hand, to find out something new, to uncover the unknown," wrote Academician V.V. Parin on the subject. He knew what he was talking about, because in his youth he himself had performed risky experiments, modestly identifying himself by his initials in the experimental data.

There are many such examples also in oncology. In one of articles written in the middle of the last century, the French dermatologists Jean Albert and Laurent Biett were described to take secretions from a patient's malignant tumour and smear it on their own skin wounds. Both remained healthy and, therefore, presumed that they had proved that cancer was not contagious.

Fonti wished to prove the reverse because she was convinced that cancer is caused by viruses. Just before the death of a female cancer patient suffering from breast cancer Fonti vigorously rubbed her own breast against the patient's festering wound. A few days later Fonti developed a severe inflammation which was at first mistaken for a tumour.

The sensationalistic press reported to the whole world that Clara Fonti had infected herself with breast cancer of her own free will. Subsequent follow-ups and successful anti-inflammatory treatment, however, made it possible to convincingly refute the hasty newspaper reports.

With due respect for the selfless action of the physician it must be explained that this experiment had been doomed to failure from the very start. Fonti proceeded from the false premise that a virus disease is contagious, just like influenza or pox; however, there are many known diseases caused by microbes or viruses that are not contagious at all. Among them are pneumonia, herpes zoster and herpes simplex (afflicting the lips). Many other examples can be found.

Cancer is not transmitted by direct contact between a patient and a healthy person. This is also true of animals. In most cases there has been no confirmation as yet of "horizontal transmission" from one individual to another. On the contrary, the spread of malignant newgrowths in animals mainly occurs through "vertical transmission"—from parents to their offspring via genetic material. An exception is chicken lymphomatosis which can be spread through the air striking groups of chicks.

Recently, the following data were reported to scientists. In a U.S. laboratory oncological tests were performed on a culture fluid containing kidney cells of healthy monkeys. In the culture fluid, which had been used to obtain a vaccine for poliomyelitis, a virus was detected which induced tumours in newborn hamsters. The virus was also found in all samples of the vaccine which had been used to inoculate infants. What kind of fate was in store for those who had been vaccinated? What awaits them?

To answer this question tests had to be performed on volunteers. Large doses of the virus failed to cause any disease, but antibodies appeared in the blood of the experimental subjects, which means that the virus had begun multiplying in the organism without producing any symptoms. All those vaccinated were specially registered and regular follow-ups are being conducted. Nothing has developed warranting concern, but at the same time the potential oncogenic hazard of the vaccine required a radical change in the technology of its preparation.

According to most contemporary researchers the insertion of the viral information into the genetic structure of the cell is only a "prelude to cancer". Even if we assume that the hypothetic virus enters the human organism through the mother's milk or with the ova of the parents ("vertical transmission") as occurs in experimental animals, it does not at all mean that a malignant tumour will appear in such a human being. The virus requires certain conditions for manifesting its pathogenicity. In this variant "vertical transmission" postulates that the offspring inherit a predisposition to precancerous conditions. The intervention of specific factors in the external and internal media is necessary for this predisposition to develop into the disease.

The increasing incidence of carcinoma of the mammary gland registered in many industrially developed countries cannot be directly linked to a more frequent penetration of the virus via the mother's milk, because the breast-feeding of children is reducing in terms of time or, in general, is being replaced by bottle-feeding. Apparently, it is not so much the viruses as the disturbance of normal hormonal activity (which was mentioned above) that is the essence of the problem.

Scientists in Novosibirsk have also confirmed this. They collected data relating to approximately 6000 females patients suffering from carcinoma of the mammary gland and studied the prevalence of malignant tumours in their daughters. The difference in the incidence of carcinoma in them as compared to that of a control group of women of corresponding age proved to be so insignificant that no conclusion could be drawn regarding the role of the "milk factor" in the development of cancer, i.e., the transmission of the virus with the mother's milk.

If cancer were really a contagious disease, it would be primarily hazardous to medical specialists, particularly oncologists who are constantly in contact with cancer patients without taking precautionary measures. Statistics show, however, that doctors and the medical personnel of cancer hospitals and institutes do not suffer a higher incidence of malignant tumours than professionals in other fields.

Today, it is so evident that the cancer patient is not contagious that in no country are oncologists financially compensated for being exposed to the hazard of infection as are specialists in infectious diseases, in venereal diseases, and phthisiologists.

Science knows of no cases where malignant tumours infection occurs between people. Doesn't the increased rate of cancer incidence in some production collectives, ethnic groups, homes and even families contradict this assertion?

We have already discussed occupational cancer. The increased incidence of these cases is caused not by contact between sick and healthy people, but by the harmful effect of various carcinogenic factors. A change in production technology that eliminates human contact with the carcinogen results in the eradication of occupational cancer.

In the Orient, the higher incidence of cancer of the oral cavity can be explained by the traditional local habit of chewing the betel or nut pas. Members of the same ethnic groups who are not addicted to this habit suffer from cancer of the oral cavity far less frequently.

About half a century ago not only the local residents, but also scientists were stunned by reports of "cancer houses" whose inhabitants died of malignant tumours. The stories that people told about these "cancer homes" were more terrifying than the rumours surrounding houses allegedly haunted by ghosts. People were afraid to move into such buildings not knowing where the danger would come from, whether it was the composition of the soil or the water, or whether the walls of such buildings harboured some particularly insidious cancer infection.

Many special investigations came to nothing until the Frenchmen A. Lumier and P. Vin proved that such frequent deaths due to cancer in one and the same house were merely coincidences; the essence of the matter was that cancer was such a widely spread disease in general.

Similar coincidences are most likely responsible for reports published abroad in recent years that leukemia affects both owners and their pets (particularly dogs) simultaneously.

Statistics involving large numbers is apt, at times, to single out, quite by chance, the occurrence of several cases of malignant tumours in one family simultaneously or in rapid succession, but "simultaneously" does not necessarily mean that one person infects another. In analyzing cancer occurring in a family it is often difficult, and sometimes impossible, to rule out the effect of identical carcinogenic factors on all the members of one family, as well as the significance of hereditary predisposition. The Soviet oncologist Professor I.T. Shevchenko contends that the risk of falling ill with cancer among relatives is much higher than among people not related by blood although both the latter and the former have lived in the same conditions, have the same customs and habits, and are exposed to similar occupational hazards as well as to other carcinogenic influences. He explains that "cancer families" exist precisely because of genetic factors.

The late Academician I.A. Kassirsky, specialising in therapeutics and haematology, summarized the reports published about leukemia occurring in twins, brothers and sisters, parents, children and grandchildren. From the data, the hereditary factor appeared to be of indisputable importance because it created a predisposition to the disease. This is confirmed by R.P. Martynova who studied 500 pairs of twins selected during an investigation of 45 000 oncological patients.

In the medical literature there is already evidence regarding the hereditary transmission of a predisposition to stomach tumours along the male line and to carcinoma of the mammary gland along the female line. Moreover, analysis of the data on twins provides significant evidence not only of the role of heredity in the origin of cancer, but of the primary role of the environment in the manifestation of the hereditary predisposition.

Retinoblastoma is a rare tumour of the retina of the eye which develops mainly in infants, sometimes even during the intrauterine period. This tumour sometimes resolves spontaneously leaving a characteristic scar on the retina. On examining the relatives of such a patient a similar scar may be encountered in an outwardly healthy parent. Statistics show that when the father or his closest relatives have been ill with the disease, the incidence of the disease in children reaches 50 per cent. Scientists believe that the predisposition to retinoblastoma depends on one single gene which determines susceptibility to a certain tumorogenic virus.

As far back as 1910, N.N. Petrov gave a very clear answer to the question whether cancer is contagious or not:

"There is no doubt that contagiousness even remotely similar to that of acknowledged contagious diseases is quite impossible. It doesn't occur to anyone anymore that the causes of the contagiousness of consumption, syphilis, or other infectious diseases need to be described. And despite the frequency of tumour development, as far as is known, nobody has yet with confirmation observed that any surgeon has become infected by a malignant tumour of a patient that he operated on.

"Statistics have shown that a married couple or people living together with cancer patients in one house are at no greater risk of contracting cancer than people living in the same city or people of the same age..."

More than seventy years have elapsed and we have nothing to add to or to alter in this statement taken from the first monograph on cancer published in the Soviet Union.

It's Too Early to Shout: "Land Ahead"

Thus, despite what might seem to be convincing data, the viral theory is still controversial. On the one hand, viruses undoubtedly have a carcinogenic role; on the other hand, they constantly take part in the ordinary life of every cell which makes it impossible to unconditionally acknowledge them to be the only source of malignant tumours. Such a contradiction stimulates further, more fundamental research, to determine the role of viruses in the complex biological processes that lead to the transformation of a normal cell into a malignant cell.

It should be emphasized once again that until very recently developments in experimental oncology depended completely on general biological research and on the potential application of its methods in special oncological projects; however, now the reverse is true, namely, the methods and techniques in experimental oncology can contribute much to biology, and, in particular, to molecular biology. This is why research in the fields of virology, genetics, and virogenetic concepts of carcinogenesis is essential to progress in biological science as such, As to the viral theory, it has actually closed ranks with the polyetiological theory advanced by Petrov about 60 years ago. The essence of the theory is that, owing to a variety of circumstances, a new "breed" of cells appears that are distinguished by their capacity for unrestrained multiplication and division. In the language of biologists this can be summed up in the following way: "Any reaction inducing cell transformation and weakening the factors that prevent the multiplication of cells may in the long run induce the development of a malignant tumour."

This concerns a major component of carcinogenesis which we have merely mentioned so far—the struggle of the organism itself against the tumour. A mass of data has already been collected and many interesting hypotheses have been developed. Many of these new concepts are well grounded, but they aspire to be universal in character, which, in our opinion, is a fundamental error. At present the immunological theory of tumour development is claiming universality.

Already in 1910, Petrov considered the lack of susceptibility to tumours proven, basing this concept on the scientific literature and on the studies he conducted jointly with his pupils S.S. Girgolav and N.I. Myslovskaya. He believed that, in principle, even prophylactic inoculations might be possible. At the same time he stressed that anti-tumoral immunity is substantially different from immunity to bacterial infection.

Although Petrov correctly posed the question so long ago, he quite naturally paid tribute to the novel ideas of his time, the time of "microbe hunters" and sensational achievements in vaccination. Everything turned out to be far more complex, although data pointing to the lack of susceptibility to injected tumours of not only individual animals, but also entire species also aroused the interest of scientists living closer to our time.

In the years 1924-1929, Academician A.A. Bogomolets, a Soviet pathophysiologist, revived the concept about the influence of the organism on the development of the tumour, primarily on its immune defence system.

For many long years immunological research in oncology played for the most part an auxiliary role in proving certain propositions of the viral carcinogenesis theory. Nevertheless, experience accumulated, methods improved, and, with the years, a lot of data was collected that attracted the interest of scholars such as the following.

During the treatment of a female patient with a diffuse form of melanoma (a very malignant skin tumour) blood that had been taken from a patient who was cured of melanoma 4 years previously was infused into her lymphatic vessels. Three weaks later the patient was again infused with blood taken from a man who was cured of melanoma 18 years before. Within two years the tumour and metastases gradually resolved and in five years the patient was healthy again.

There have been similarly significant observations of patients suffering from intraepithelial carcinoma known as carcinoma *in situ*. In such tumours one can find subtle morphological traces of malignancy with the exception of the most important feature—penetrating, infiltrative growth.

Many researchers consider these to be precancerous growths, but there exists the term "compensated cancer", so far as the "non-malignant"behaviour of the newgrowths depends on their interrelation with the organism and on the organism's anti-tumoral response. When the defense mechanisms weaken, the established equilibrium is disturbed and the disease triumphs.

In 1972, the Leningrad scientists F.V. Balluzek and V.I. Pechersky wrote: "The indisputable value of the immunological concept of carcinogenesis lies in its integration of all former scientific hypotheses that explain the natural patterns of tumour growth." This evaluation arose from the desire to generalize. Süss, Kinsel and Scribner noted skeptically that no science is free of hasty judgements and prejudices, and oncology is certainly no exception to the rule. Due to the wide range of its observations, which, moreover, are remarkably removed from one another, oncology, more than any other science, stands in need of (let this be an exaggeration, but nonetheless containing some truth) inspiring faith in a hypothesis that can lay an even barely noticeable path through the dense maze of as yet unconformable facts and concepts.

Before we describe the immunological concept of carcinogenesis, let us dwell briefly on immunology itself.

The natural defenses of the organism were discovered when infectious diseases began to be studied. It was established at the time that if foreign protein or polysaccharide substances (antigens) find their way into the organism (as microbes do, for instance), antibodies are produced which come into contact with the antigen and render it harmless. This happens through a sequence of fairly complicated processes which are now known in detail. Later it became clear that some antigens are constantly present in the organism and manifest their presence only under certain conditions. Among them is the rhesus factor. How was it discovered? Blood transfusions of compatible blood groups, particularly repeated transfusions, sometimes ended in pathological states for which no explanation could be found. It was finally revealed that some people always have antigens in their blood: they were demonstrated in experiments with the blood of rhesus monkeys, which lent the name to this factor. If the blood of an individual containing the rhesus factor is transfused into a person with "pure" blood, the latter produces antibodies to this factor; a repeated transfusion of the same blood results in an encounter of the antigen with the antibody creating a severe general reaction. This is how evidence was obtained of the fact that immunity is directed not only against infection.

The latter half of our century has been marked by the rapid development in the field of the immunology of non-infectious disease. This time the "boom" in immunology produced transplantology, which is the science of transplanting organs and tissues.

Van Helmont, a Flemish physician who lived in the 17th century, recorded a curious story: "A citizen of Brussels who had lost his nose in battle appealed to the famous surgeon Tagliacozzi in Bologna to fix him with a new nose. Since he was afraid to have his arm cut to supply body tissues for transplantation, he paid another man to have the new nose cut out from his flesh and the operation was performed. Thirteen months later, however, after the patient had already returned home, the transplanted nose suddenly began to grow cold, to decay, and in a few days simply fell off. When trying to find the reason for this failure the patient's friends learned that precisely at the time when the transplanted nose had begun to disintegrate, the donor had died. Respected citizens of Brussels who are alive to this day may testify to the truth of this incident..."

If we ignore the mystical connotation related to the simultaneous timing of the death of the donor and the nose, it can be considered that a very accurate description of the reaction of rejection had already been given in the 17th century.

On December 3, 1967 the whole world was stunned by the news of the first heart transplant operation performed by surgeons in Capetown, South Africa, under the supervision of Dr. Christiaan Barnard. Health bulletins about all his transplant patients were subsequently published in the press and announced over radio and television. Many medical topics which had formerly been discussed only by specialists now reached the general public.

When the sensational headlines disappeared from the newspapers, however, reports and articles about transplants, that dealt with both its successes and failures, appeared in their proper place—in scientific journals. Barnard's operations nevertheless inspired a series of similar operations in other countries and stimulated research in immunology.

Without delving into the complex and not always convincing theoretical questions, it should be mentioned that fairly recently substances were found that suppressed the immunological reaction of the recipient to transplants, and their appropriate use created the necessary prerequisites for successful transplant surgery in clinical practice.

Researcher's concepts considerably broadened and the eminent Australian immunologist Barnett advanced a theory according to which immunological self-recognition is considered a derivative of the process that permits the maintenance of morphological and functional unity in large and long-living multicellular organisms.

One can only wonder what a strange creature man is! He scrupulously protects his biological individuality, rejecting, keeping away and suppressing even the tiniest alien cell, but he absorbs like a sponge alien thoughts, opinions and experience...

Scientists found it inadequate simply to know that antigens in the organism encounter antibodies that are called upon to either destroy or remove the uninvited agent. They began investigating how this occurs and came up with rather interesting detailed information.

The stability of the inner medium of the organism is also ensured against infection or its "own" enemies, i.e., its own cells whose antigenic properties have changed owing to a variety of reasons, including the results of exposure to radiation, chemicals and viruses.

For this purpose the organism must have structural elements capable of distinguishing "their own" from "alien" and of destroying the alien. This function is fulfilled by lymphoid cells.

It has been known for some time that antibodies are formed by plasma cells and that the concrete task of immune lymphocytes consists in freeing the organism from "newcomers". In the last ten years scientists succeeded in revealing the secrets of extremely complicated multistage cellular transformations and interrelations. A new science was thus born which as yet possesses only the following principal facts at its disposal.

The lymphocytes are small cells with a big nucleus which are constantly present in the blood. They are not at all homogeneous in their functional properties; they are "supplied" by different components of the haemopoietic system such as the bone marrow, lymph nodes, spleen and thymus, which is located behind the breast bone. In the small lymphocytes, which are formed in the bone marrow, sensitive areas of the membranes (receptors) were discovered—these are the first to come in contact with and recognize alien antigens. The process of recognition triggers the transformation of these cells (called B-cells) into plasmocytes, which produce antibodies. However, they can do nothing alone, without the other lymphocytes formed in the thymus (they are called T-lymphocytes). This is a type of "insurance" system.

Researchers gradually came to the conclusion that these two systems are also not homogeneous: there are many smaller subdivisions, the number of which increase in the process of an immunological reaction. There are helper cells, killer cells and so on, to the extent that a remote control system exists (active substances circulating in the tissue fluids of the organism are responsible for this system). Furthermore, the B-lymphocytes and T-lymphocytes do not really "insure" one another but rather they divide the functions; namely, the B-lymphocytes are responsible for all the types of immune responses, but they are controlled by T-lymphocytes and other mechanisms, while T-lymphocytes fight against the antigens of tissue incompatibility resulting from tissue and organ transplants and also against the "internal enemies" (to use the expression of B.D. Brondz and O.V. Rokhlin)—their own cells which have undergone profound changes under this or that influence.

It is notable that antibodies are formed "under the inspection" of a large number of genes intricately connected with one another. In this way immunology joins with another science—genetics. Thus, new, truly boundless horizons are opened for scientific research. On the other hand, it is still obvious that it would be fruitless at this stage to seek a unified integrating theory.

What relation has this to the secret of the origin of cancer which commands our interest? There is a direct connection, for, as it has been stated above, immunology dominates in theoretical oncology today.

In the number of its followers and the number of experiments carried out to reveal its details, the position held by immunology in science is historically comparable to that of Rudolph Virchow's stimulation theory. In 1975, in a most enlightening article, Academician R.E. Kavetsky wrote that in our time, after the classic works of L.A. Silber, G.I. Abelev, Morton, Klein and many others, nobody can doubt the antigenic distinctions of the tumour cell compared to a corresponding normal cell. Since there are antigenic distinctions, immunological surveillance must appear too in the form of certain humoral or cellular reactions.

Virchow asserted that no one, even if placed under torture, would actually be able to define what a tumour cell is. Süss, Kinsel and Scribner, whom we are always citing, nonetheless attempted to formulate a preliminary definition stating that, in the simplest case, a cell may be considered tumoral if it divides more often than its neighbouring cells. Frequent division, however, is not sufficient for the organism to regard this cell as "alien" and to interfere in intracellular functioning. The same authors reason further that it is believed that the immune defense system of the host begins to function only when tumour cells already exist and that no one doubts that in order to understand how tumour cells appear, it is absolutely necessary to study immune reactions.

The contradiction is obvious, but they very cautiously avoid it. As a matter of fact, the question of which comes first—tumoral growth or immunological reaction—is a principal one for oncology. If immunodepression occurs first, then the study of tumour immunology may yield a solution to the problem and help to develop preventive measures. If everything occurs in reverse, then the recognition of the immunological failure of oncological patients and animals with malignant new growths may be of no greater importance than the knowledge that leucocytosis and a high ESR are typical of inflammatory diseases, but do not explain their essence.

There is sufficient evidence defending both points of view. Let us examine them briefly, proceeding from the latest research of mainly Soviet scientists.

Before all else, it must be clarified whether or not the tumour cells possess distinctions that ensure the immunological response of the organism.

Already in the beginning of the 1970s it seemed that there must be some kind of biochemical substance that characterizes tumoral properties. Why couldn't it be a specific antigen?

Professor V.S. Shapot, the eminent biochemist (to whom we have already referred), considers that there are no basic biochemical distinctions: "... not a single case has been discovered of tumour cells containing any kind of specific, biochemically characterised protein, enzyme or new enzymatic reactions which are not inherent in normal cells in one or another period of their oncogenetic development. This has proved that there are no antigens in human tumours that could not be detected during the normal embryonal development of the tissues. There is no genetic defect, inherent to all malignant tumours, manifested in the form of a loss, or, on the contrary, an appearance of a new product coded by this or that gene."

Researchers already have facts at their disposal that prove that tumours without antigens exist, as well as tumours whose antigenic properties are lost with time, although they continue to remain malignant.

Professor A.I. Ageyenko, another Soviet oncologist, is of the opinion that immunological changes attending malignant transformation (the transformation of an initially normal cell into a cancerous cell) are a most subtle reflection of biochemical shifts in the cell. In other words, immunological changes are a consequence, not a cause, of transformation.

At the same time, in recent years much new data has been collected which appear to indisputably testify to the participation of immunological factors in carcinogenesis.

The diagnosis of tumours of the liver by conventional and X-ray methods is very difficult. The identification of early forms, particularly if the nodus of the tumour is somewhere in the centre or on the posterior surface of the organ, is practically impossible.

For a long time the biochemist Yu.S. Tatarinov studied antigens in the blood serum of the human fetus. By applying sophisticated biochemical and electrochemical methods, he succeeded in separating three specific antigenic components distinguished by their mobility in an electric field. In Abelev's laboratory, which specializes in immunology, it was established that one of the components of fetal serum (ESP—glycoprotein) is identical to the glycoprotein detected earlier by Tatarinov in the blood of patients suffering from carcinoma of the liver. Joint efforts by both laboratories proved that this substance is absent in the serum of healthy adults, but present during a specific form of cancer of the liver. The reaction discovered by Abelev and Tatarinov was tested both in the USSR and, by decision of the WHO, in some African countries where cancer of the liver occurs frequently. The results testify to the high reliability of the test. This discovery is not only of practical significance. It is very important because it confirms, in principle, the possibility of using an immunological test for the diagnosis of malignant tumours.

In 1958 a group of Soviet scientists headed by L.A. Silber (V.V. Gorodilova, Z.M. Sarayeva and I.G. Silina) attempted to produce active immunity in patients with carcinoma of the mammary gland. Two groups of patients (50 in each group) at the same stage of the disease were taken under observation. One group underwent conventional treatment, i.e., radiation therapy and surgery. In addition to the same treatment, patients in the second group were infused with lysed (killed) cells taken from their own tumour or from the tumour of another patient. Ten years later 51.2 per cent of the vaccinated (infused) females were still alive, while among patients who had undergone only the conventional combined treatment only 28.7 per cent survived. Although this evidence requires further analysis and corroboration, it demands a serious approach to the problem of the immunology of tumours. The comparably small number of observations were not sufficient to make definite conclusions.

In the history of science there are many such examples. At the beginning of this century the physiologist Alexis Carrel, the first American scientist to win the Nobel prize, removed both kidneys from a dog and transplanted the kidney of another dog without taking precautionary measures to suppress tissue rejection. The experimental animal lived 4 years. No one, not even Carrel himself, succeeded in repeating this unique experiment. Most probably the results were due to a most rare coincidence of two compatible animals.

We discussed above that some scholars think that the cells of a malignant neoplasm originate from normal cells and by all indications remain as the cells of a diseased organism. However, there is another point of view.

Adherents of the immunological theory of cancer are inclined to think that tumour cells appear in the organism continuously. The cells are identified by the immune system as "alien" and are destroyed by the usual rejection response, i.e., the same reaction which does not "accept" an alien transplanted organ. Incidentally, this theory is based on the fact noted by physicians specializing in transplant surgery that there is a higher incidence of malignant tumours in patients who received drugs suppressing the defense forces of the organism.

The famous American surgeon F. Moore cites the following case. One of his patients received a kidney transplant that contained the metastases of lung cancer. These metastases began to spread rapidly because of treatment with immunodepressants. When immunodepressant therapy was stopped, the organism rapidly and completely rejected the transplanted kidney with its tumour. Later, the patient successively underwent another transplant operation. Tumoral growth was no longer observed.

A number of Soviet scientists also managed to obtain convincing evidence of the functioning of immunological factors in carcinogenesis. This theory attracted the attention of not only researchers, but also clinical practitioners, as was demonstrated by one of the conferences of the Moscow Oncological Society devoted to anti-tumoral immunity. This conference was held about 8 years ago at the P.A. Herzen Institute where the first experimental laboratory in virology and immunology had been set up after World War Two. This laboratory, the first of its kind in the world, was headed by L.A. Silber.

The discussions at this conference dealt with profound theoretical questions much too complex for the ordinary public, yet the hall was packed. Clinical physicians with keen interest followed the debate led by the leading Soviet immunologists G.I. Abelev, G.I. Adveyev, V.M. Bergolts and G.I. Deutschman. The clinical oncologists hoped that an immunological approach to cancer might open up new horizons in the theory of carcinogenesis as well as in the diagnostics and the treatment of malignant tumours. The experimental researchers, however, warned their listeners against drawing hasty conclusions.

In fact, fundamental distinctions between healthy and tumour cells have as yet been found only in the unrestrained division of tumour cells, which may be explained by certain peculiar features of their membranes.

Let us illustrate this by an analogous example from daily life. Imagine that you are driving a car with excellent brakes. Suddenly, however, air enters the brake system. An experienced driver will grasp the hand brake and change into low gear. A driver with no experience will not be able to slow down and the car will go speeding ahead. Tumour cells also lose contact with the braking systems and continue to multiply needlessly, causing the organism harm; however, in principle, the biochemical structure of tumour cells is no different from healthy cells. Returning to the analogous example, the uncontrolled car has the same structure and the same defect as the driven car, but it is the absence of control that leads to catastrophe.

This comparison leads us to believe that a cell that has already been transformed actually has no chance to acquire specific antigenic properties. Thus, the immunological changes that appear are the consequence and not the cause of transformation. Not every one, however, is in agreement with this.

Professor V.V. Gorodilova, a consistent and convinced advocate of the role of immunological processes in carcinogenesis believes that oncogenic factors are responsible for the development of tumours, but that they first suppress the immune defenses of the organism and it is exclusively on this condition that the malignant transformation of cells becomes possible. The fate of the tumour depends on the force and efficacy of the body's response to tumoral growth.

In any case, the participation of immunological mechanisms in the development of the tumour is indisputable. The question that remains is whether the defense reaction determines everything or whether it is merely one of many factors that must be taken into account.

In order to understand how the tumour develops, the three stages of tumour growth should be discussed. Scholars give different names to these stages, but the essence remains the same. The description given by R.E. Kavetsky is the most precise.

Stage I. Initiation—transformation (conversion) of the normal cell into a potential tumour cell; the functions of its genetic apparatus change, but it is still incapable of tumoral growth.

Stage II. Activation, or stimulation. Under the influence of non-specific ("non-carcinogenic") factors, some of the transformed cells become activated and begin to multiply.

Stage III. Progression. The tumour grows rapidly with proliferation of tissues and metastasis due to the breakdown of defense mechanisms.

The first two stages—initiation and stimulation—take place at the level of the cell or group of cells with no sign of any morbid manifestations. In practice it is very difficult to "examine" these stages; so far success has been achieved only in tissue cultures, that is, in cells artificially "displaced" from the organism. This is why the study of immunological reactions during these two stages is of purely theoretical interest. In the clinic today immunological reactions can be investigated only at the third stage.

Advocates of the immunological theory offer the following arguments: first of all, there are known cases of spontaneous regression of tumours and metastases, documented in clinical experiments. Second, there is a higher incidence of tumours among individuals who have undergone immunodepressive therapy following organ transplants (e.g., kidney transplants). Third, in congenital and acquired diseases connected with an insufficiency of the immune defense system there is also a higher incidence of malignant neoplasms. For example, many lymphatic tumours occur most frequently among those people who do not have enough, or who completely lack, proteins in their blood—the carriers of immune defense.

Moreover, tumours often appear in organs that are isolated from the action of immune mechanisms (the lens of the eye, the brain, the thyroid gland, etc.). Finally, the advocates of this theory believe that the organism may develop immunological tolerance in regard to the tumour.

It is interesting to examine these arguments from the point of view of physicians who daily come in contact with cancer patients and know the results of clinical statistical research.

The spontaneous regression of tumours and metastases is not the rule, but rather a very rare exception: therefore, such an uncommon phenomenon cannot be taken as the basis for generalization. It is characteristic that Professor V.I. Govalo, who is actively conducting research in the field of tumour immunology, refrains from using this argument in his book.

According to the data of the American doctor Penn and coworkers, out of 9131 kidney transplant and 189 heart transplant patients, during the first 30 months after transplantation and initiation of drug suppression of the immune defense system, tumours developed in 95 patients. This is a several times higher incidence than that encountered in people of the same age (the average age of patients was 36 years). The ratio of the incidence of different forms of the tumour was also completely different from that found in patients who had spontaneously become ill. The tumours were mainly of non-epithelial origin—reticular sarcoma. Along with lymphomas they occurred in nearly one-third of the patients, while they usually account for an insignificant fraction of the incidence.

It has been established that immunodepressive therapy alone, during various disease states, is also conducive to tumoral growth, but is a considerably rarer occurrence (by an entire order of magnitude) than in transplant operations. Evidently the transplant operation itself, which induces the reaction of the "transplant against the host", depresses immunity.

The crux of the matter is that cancer, which appears during immunodepression, is not inclined to be "aggressive" and is quite successfully cured by local mechanisms. How can this be explained if the immunological factor is recognised as the leading one in tumoral progression?

In diseases that are connected with immunological insufficiency (most often congenital pathology, genetically transmitted) the same rule applies as in transplants—tumours of connective-tissue origin appear. This fact, therefore, in no way explains the prevalence of such tumours as carcinoma of the stomach, lung, skin, and mammary gland.

Tumours of the lens of the eye, brain and thyroid gland are generally highly unusual occurrences. Tumours of the brain account for 4.7 to 8 per cent of all malignant diseases, cancer of the thyroid gland, just

1 per cent, while carcinoma of the lens of the eye is such a rare occurrence that it is not even mentioned in reference books on oncology. If the absence of immunological defenses really determines the appearance and development of tumours, then lesions of these organs would dominate statistically, but this is not the case.

The Soviet researcher V.Ya. Shats published a review entitled *Immunological Paralysis in Tumour Growth* where he summed up a vast amount of scrupulously analyzed scientific data on tolerance, which had been collected over the last ten years. He concluded:

"...Immunological paralysis in tumour growth is possible, but its significance should not be overestimated. This condition cannot be brought to light by known methods...

"...If tolerance develops to every new tissue that appears in the organism with altered antigens, the immunological surveillance system loses meaning and will stop functioning."

Shats adds: "Immunological paralysis is a possible, but evidently not an obligatory, part of the immunological response to the tumour."

In the review a question is quoted that was raised by Professor Alexander of England, a supporter of the immunological theory. He asked why tumours continue to grow if tolerance plays no role in the processes of tumour growth.

Thus, after so much effort, only a feeble question can be raised. And Alexander is not alone. In 1974 Yu.M. Vasilyev, the most eminent Soviet researcher in the field of carcinogenesis, unambiguously declared that the participation of immune reactions in the development and growth of tumours in man is still not clear. Scholars all over the world are still tackling this problem.

As it has occurred in medicine time and again, the lack of persuasiveness and controversial nature of theoretical opinions do not prevent attempts to apply already uncovered natural mechanisms to save the lives of patients.

To illustrate this point, let us return to transplant surgery. For many years the possibility of organ transplants was studied only experimentally. The data stubbornly testified to the endless difficulties involved in overcoming the barrier of tissue incompatibility. In general, researchers managed to outline possible approaches, but the transplants died just as frequently as before, often killing experimental animals in the process. Nevertheless, twenty years ago, the accumulated experience made it possible for Academician B.V. Petrovsky, Yu.M. Lopukhin and the foreign specialists Merill, Amburge and others to begin serious clinical research on humans originating from the acute need to help patients with absolutely hopeless prognoses due to loss of function in both kidneys.

With modern drugs and technical devices the barrier of incompatibility may be overcome, and we are currently witnessing tremendous successes in transplant surgery, although many theoretical concepts still require additional research.

The situation is precisely the same in the field of tumour immunology. For many years now researchers have been trying to use immunological reactions in diagnostic applications, mainly to detect cancer in its early stages. The determination of the general non-specific reactivity of the organism, which is an important factor in prognosis both in oncology and in medicine as a whole, is the central issue.

Already thirty years ago the retarded hypersensitivity reaction and the determination of capillary permeability were used to predict outbreaks of latent infection connected with surgery. T.A. Kunitsyna, E.I. Malyukov, I. Teodorescu and others proved that a depression in general immunity considerably heightens the risk of surgical intervention. According to Kunitsyna and Malyukov, a number of methods recommended by clinical immunologists for studying the condition of cancer patients may be adequately applied as tests to determine purulent complications in the post-operative period. These and other tests give an overall evaluation of the condition of the immune system, and therefore, of the prognosis. As for diagnosis, V.V. Gorodilova correctly points out that tumours of various etiology are encountered in man. Should they be of viral origin, both immunodiagnostics and immunotherapy will evidently be applicable.

It is proposed that non-specific "reactions to cancer" should not be sought, but it should be estimated to what extent the organism mobilizes defense mechanisms that take part in pathological processes irrespective of their nature (inflammation, tuberculosis, cancer, etc.). Scientists believe that should they discover defects in this system, scrupulous investigation will be able to detect cancer at this period, when there are as yet no obvious clinical symptoms of the disease. The first successes have already been achieved in this direction.

The international oncological literature is overflowing with reports of attempts to treat tumours by immunotherapy. Two approaches have taken shape. One group of oncologists is attempting to increase the defense forces of the patient's organism by non-specific stimulation using vaccines, killed or weakened microbes, etc. The principle is far from new. Already in the 1920s, physicians knew that smallpox vaccinations are effective not only against smallpox, but against all fevers in general, because they activate phagocytosis. Activated phagocytosis is also frequently achieved now whenever immunotherapy is applied to cancer. A second group of oncologists continues to investigate where the defect in the complicated immune system has occurred, so as to repair the rupture. The path is not smooth for either group, but nevertheless they manage to some extent to improve the fate of severely ill patients.

On the other hand, in 1973, Academician R.E. Kavetsky wrote that any attempt to immunize or vaccinate cancer patients at the height of the disease is doomed to failure because the organism is already saturated with tumoral antigens and reactivity is depressed. It must first be liberated from the mass of tumour cells and the immunogenesis system must be "revived", and only then can vaccination be attempted. Attention must be focussed not only on anti-tumour defense but also on the restoration of reactivity as such.

This general conclusion by the eminent scholar helps to explain why achievements in immunotherapy are still so modest. Theory and practice in this field are also advancing so slowly because immunotherapy may sometimes have a negative effect on the development of the disease, and this makes researchers extremely cautious in its application.

The French oncologist George Mathé, one of the original researchers in immunotherapy, warned that even if immunotherapy develops into an effective therapeutic method, it will still be very difficult to use.

Moreover, an important factor linked

with one of the natural mechanisms mentioned above is of great significance. Let us enumerate the malignant diseases of man in which immunotherapy has some effect: leukemia, Burkitt's lymphoma, sarcoma, melanoma, chorion-epithelioma. All of these diseases have no relation to epithelial tumours, that is, to cancer. It is a curious fact that during immunodepression in humans, as has been noted, most often malignant diseases of non-epithelial origin develop, for which immunotherapy has turned out to be effective treatment. This circumstance again emphasizes the complexity of transferring to the clinic those natural mechanisms which were established by experiment: the majority of experimental tumours are not identical to cancer arising in humans.

It was stated above that immunology is now aspiring to be an integrative science removing the contradictions of other theories. However, matters are probably different—there is no theory of oncology as yet which can embrace and explain everything. This does not mean that it is no longer necessary to investigate the immunology of tumours. All the systems maintaining the internal medium of the organism must be studied: the endocrine system, nervous system, and the system of active connective tissue.

Professor I.P. Tereshchenko of the Herzen Oncological Institute in Moscow traced the close connection of endocrine disorders with the condition of the immune defense system, as well as with the genetically determined resistance or predisposition to tumoral growth in experimental animals. V.S. Shapot was able to "build a bridge" connecting biochemical and genetic research that gave strength to serious doubts concerning the mutation theory of carcinogenesis.

There are many such examples in Soviet and international experimental oncology: they reflect the objective development of science and stimulate new investigations. Apparently, however, the period of synthesizing knowledge has not yet begun that could yield a universal theory.

This assertion should not give rise to pessimism. What we know about cancer to date assists us in combatting the disease effectively. There may be many points of view regarding the origin of cancer, but it has been established that up to 70 per cent of malignant tumours in man are induced by chemical carcinogens. This confirms that the struggle waged against the pollution of our environment is in itself the real prevention of many forms of cancer.

Our possibilities are not limited by this situation. Today, we know for certain that if a tumour is recognized at an early stage before metastasis sets in, in the majority of cases it can be completely cured. In the first stage of cervical carcinoma radiation therapy alone, just as only one operation, cures 90 per cent of all patients. Operations performed during the first stage of carcinoma of the mammary gland produces the same results. Even in carcinoma of the stomach, radical intervention, when only the mucosa has been affected (the true first stage), produces a similar result: approximately 90 per cent of all patients are cured.[1]

This is why the timely detection of a tumour and the correct choice of optimal therapeutic approaches are no less important than the search for pathogenetic methods of treatment. All these types of investigations are being conducted in parallel. Their successes are indisputable and we shall discuss them in later chapters of this book. Theory and practice are being mutually enriched.

Thus, the discussion of many questions in theoretical oncology results in ambiguity. A superficial acquaintance with this or that theory, this or that group of facts, may give the impression that the key to the problem is precisely here and just a bit more effort will reveal how cancer can be prevented or at least give hope of curing the disease, of intervening in complex biological processes to benefit people. A closer examination of these theories, however, proves that the natural mechanisms uncovered by hard work do not possess universal significance in carcinogenesis, that a given theory is only one of many hypotheses that may be firmly refuted, or at least questioned or doubted with good reason. Indisputable facts remain that only describe certain fragments of the process and fail to reveal the nature of the phenomenon in all its complexity. The development of theoretical oncology is probably the most mysterious page in the history of biological science, a page that is far from complete.

In his book *Man Against Cancer* Glemser writes that scientists engaged in cancer research are swamped with problems. They are remarkable people and to the outsider they may seem to be from a different world. How many more years will these scholars have to toil in this manner? Fifty, or two hundred and fifty years? No one can say. They are so deeply involved in their work conducting research on enzymes, nucleic acids, and cellular membranes, and digging into statistics about carcinoma of the liver among the Bantu tribe, about the effect that the habit of chewing seal skin produces in Alaskan women, that they have no time to even think about anything else; they dedicate themselves completely to the problem at hand. The human race is not so bad, after all, if it gave the world such fighters against cancer. Glemser states that he is full of admiration for these people, that they perform miracles, and that he is proud to belong to the same human race.

Iskander's Grandson

The Herzen Research Oncological Institute is located in the centre of Moscow at the intersection of Begovaya Street and 2nd Botkin Street. It is named not after Alexander Herzen, the great Russian revolutionary, writer and philosopher, but after his grandson Peter Herzen.

In the Soviet Encyclopaedia grandfather and grandson are listed one after the other. Between them, another name has been unfairly omitted, that of Alexander Alexandrovich Herzen—the son of the philosopher, famous in his own right as a physiologist, well-known in his time, and with whom the famous I.M. Sechenov engaged in polemics about science. The three generations of Herzens make one doubt the correctness of the genetic postulate that nature, having generously endowed one representative of a family, economizes on the rest.

In a brilliant article on the centennial of A.I. Herzen, Vladimir Lenin underscored that the worker's party must honour Herzen not out of philistine glorification, but for the purpose of defining its tasks and clarifying the true historical significance of the writer who played a great role in preparing the Russian revolution.

With the same purposeful attitude, the colleagues, pupils and numerous followers of P.A. Herzen gathered together in 1971 to celebrate the centennial of the scientist's birth. In order to correctly evaluate the progress made in the science to which P.A. Herzen devoted his entire life, one has only to compare two facts: the institute bearing his name today was founded in 1903 as a hospital for incurable cancer patients (there were almost no curable cancer patients at the time); and the high point of the anniversary session of the Institute commemorating 75 years since its foundation was the discussion about early forms of cancer that are now treated with an almost 100 per cent recovery rate. As they projected new frontiers in their research, oncologists gratefully remembered P.A. Herzen for his immense foresight and infectious optimism.

Do we have the right, however, to connect grandfather and grandson with greater ties than kinship? In fact they never actually met: Peter Herzen was born nearly 18 months after the death of Alexander Herzen. The personality of Alexander Herzen was so outstanding, however, and the ideas outlined in his philosophical and literary works were so attractive, that they have favourably influenced and continue to have a positive effect on more than one generation of young people. It is obvious that such an influence was bound to have an impact on the fate of Herzen's grandson.

Let us consider the question of choice of profession. The cult of natural sciences reigned in the Herzen family. Not knowing the sciences, A.I. Herzen claimed, one is not insured against mystical beliefs. When he was working on *Letters About Nature Studies* Herzen himself attended lectures delivered by Professor I.T. Glebov on zoology and anatomy at Moscow University. Although he was born and raised among aristocrats and snobs, Herzen had the highest respect for the professions of doctor, surgeon and naturalist, and in his youth he nearly chose to become a physician. It is no wonder that his favourite hero in fiction was Doctor Krupov.

Alexander Herzen was personally acquainted with many famous physicians who became his friends and whose names are often mentioned in his memoirs and letters. First among these was Sergei Botkin, whom Herzen met in Paris and whose talents he immediately recognized, exclaiming, "I have never met such a doctor." Among others were the Russian physician Vasily Neftel, the Italian Basilio, who went to England in 1864 with Garibaldi, the French neurosurgeon P. Broca, who was the physician to the Herzen family, and the Frenchman Deville, who performed surgery on Ogarev. Alexander Herzen described this obviously not very serious operation: "Deville is very skilled. I was present during surgery. It lasted a mere two minutes..." Herzen was friends with many other doctors.

The physician must be a humanist such as Dr. Haaz was. "His name should not be lost in the welter of official obituaries," wrote Alexander Herzen.

A real doctor is always ready to sacrifice his own health, even his life to save a patient. For many long years Alexander Herzen was to remember the selfless behaviour of the medical students of Moscow University during a cholera epidemic. Later, when Paris succumbed to cholera, Herzen himself displayed great courage, remaining alone to attend to Ivan Turgenev who was stricken by the disease, to look after him until he was well again.

The profession of a physician is incompatible with cruelty. A.I. Herzen branded F.I. Iyelalich, a professor at Kazan University who advocated "skin surgery", a "plantation slavemaster" for being so harsh with the serfs on his lands.

According to Alexander Herzen, the true physician must have a broad outlook, well thought-out actions, and a scientific approach to every patient. N.I. Pirogov precisely lived up to these standards. In describing him, A.I. Herzen used only the most laudable epithets, calling him a famous surgeon and the most erudite physician in all of Europe. He considered Pirogov to be one of the most outstanding graduates of Moscow University on a level with Lermontov, Belinsky, Turgenev and Kavelin. Visitors to the London home of Herzen testify that Pirogov's portrait hung in the most visible and honoured place—among the portraits of the Decembrists.

A.I. Herzen regarded surgery as one of the crowning glories of medicine and predicted a great future for this specialty. He wanted his son Alexander to follow in the steps of Pirogov, but this wish was fulfilled by his grandson. It so happened that Peter Herzen realized and embodied many of the legacies that Alexander Herzen had left to his son.

"Six-seven troikas escorted us to the village of Chornaya Gryaz... where we drank a toast and said farewell in tears," recalled A.I. Herzen when he fled from Tsar Nikolai's Russia in January 1847. It was only after he had crossed the border that it became possible for him to continue struggling openly against tsarist rule and serfdom.

Having emigrated, however, A.I. Herzen never for a moment felt that he was an outcast of his beloved motherland. From early youth his heart and soul nurtured that "powerful, physiological, passionate feeling... a boundless feeling, engulfing his very existence, of love for the Russian people, Russian life and Russian way of thinking..." This is why, in choosing his land of exile, Herzen did not go to prosperous America, which, like Garibaldi, he called "the land of one's forgotten motherland".

Living outside his homeland meant, to use his expression, "making a sacrifice, an enormous sacrifice for our cause."

Nostalgia never left Herzen. Even 13 years after emigration he still could not become used to his land of exile and in the preface to his memoirs, *My Past and Thoughts*, he wrote: "Around me everything has changed, the Thames instead of Moskva River and an alien tribe among whom I live. There is no longer a road back home for us..." During moments of gloom Alexander Herzen was sustained by the feeling that there were "his own people in Russia" who would readily embrace his successors. "Return to Russia if possible, you belong there," he advised his son.

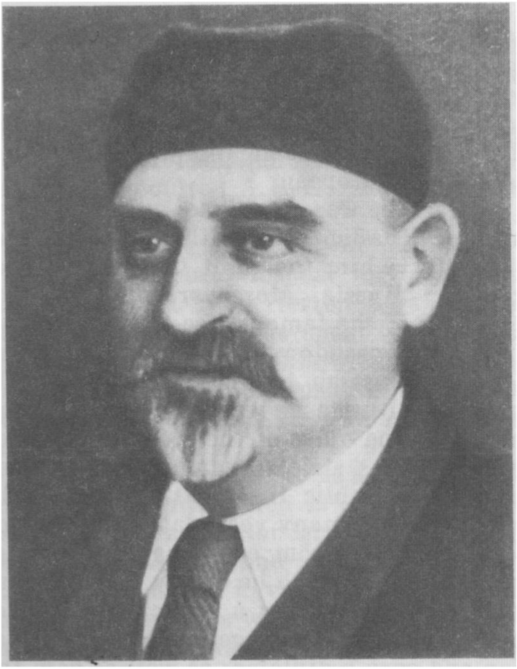
"The return to the motherland" was the recurring theme in Herzen's correspondence with his children. "...I am again beginning to think that the time will come when you can simply go to Russia as a naturalist," he wrote in another letter.

The entire programme of his life, actually, his moral testament is expressed, in essence, in the following quote: "The religion of future social reconstruction is the only religion I impart to you... Return in time to our home to preach it. There was a time when they loved my language and perhaps they will remember me. I bless you to embark upon this road in the name of human reason, personal freedom and fraternal love!"

In October 1852 Herzen exhorts his eight-year-old daughter: "I am very glad that you can write in French, my dear Tata, but it is most important that you always speak in Russian. You are a Russian girl and must teach Olya (her two-year-old sister—*Author*) Russian. Having noticed that the children were gradually assimilating the culture around them and forgetting their own, he bitterly admitted: "In your foreign circle of friends, I am the foreigner," —this should be read as, "the Russian patriot".

It is said that when Alexander Herzen was dying from pneumonia the last words that he spoke while still with a clear mind were of his homeland: "Why not go back to Russia?" His children could not (or did not want to) comply with his behest, but exactly 50 years after Herzen's forced emigration, his 26-year-old grandson, who had become a very promising assistant to the world-famous Swiss surgeon Professor César Roux, crossed the border of Russia in the reverse direction.

Peter Herzen returned to his grandfather's homeland, but not in a troika; he came back in a comfortable railway car. The feudal Russia which Alexander Herzen had left within a period of half a century was rapidly becoming a capitalist country, covered by a network of railroads. The revolutionary class was maturing and gaining strength. Much had changed and not without



P.A. HERZEN

the participation of Alexander Herzen.

Photographs reveal what Peter Herzen looked like in his youth. His large brown eyes under bushy dark eyebrows are piercing. An aquiline nose like an eagle's beak above a goatee (not yet grey as in later years), and abundant whiskers. The hair on his face distracts from his bald spot, blending with a high proud brow usually likened to that of Socrates. His bow tie is the finishing touch to the elegant artistic portrait. In the photograph Peter Herzen looks older than his years and his appearance is definitely European.

In fact, he was a foreigner with no knowledge of Russian, and with a diploma that did not give him the right to practice medicine in Russia. Moreover, he was the grandson of the famous free-thinker, known under the pseudonym Iskander, who had become a pariah to his own country. On arrival in Russia he was immediately summoned to the office of the Moscow governor where he was strictly admonished to keep out of the public limelight. It should be added that for many years later his surname prevented him from engaging in teaching, an occupation which he dearly loved. Meanwhile, he had to start a new career all over again, learn the language, defend a dissertation and earn a diploma, as well as gain the respect of his colleagues and patients.

Peter Herzen fully realized that the best way to master the language was by close association with native Russians, therefore, for several months he chose voluntary exile in the hinterlands near Vetluga, taking up residence at the estate of V.F. Luginin, a professor at Moscow University, who founded the first thermochemical laboratory in Russia and whose works are still considered exemplary models for the precision of measurements and calculations given in them. Luginin was also a scholar of progressive views. In the sixties he had been an emigré, working for the publication of *The Kolokol* (or *Bell*). At one time he had also courted A.I. Herzen's daughter Natalie.

Here, in the home of an old family friend, from a rural teacher and the peasants of Vetluga, Peter Herzen began studying Russian. Later, he spent the rest of his life perfecting his knowledge, reading the great literature of Pushkin, Turgenev, Tolstoi, Chekhov and his own grandfather in the original.

Peter Herzen proved to be a very capable language student, which is clearly seen in the articles and monographs he wrote. Just as Dr. Krupov had stated in his time, P.A. Herzen might have said that the purpose of his writings was not to be literary, but to be of informational value in pathology; he did not wish to captivate his reader, but to be useful to him. Yet, P.A. Herzen's scientific works are written in good style. It was only when speaking that his accent revealed that he had not learned Russian from childhood. It stuck in everyone's memory, when listening to his temperamental speech, the peculiar way he pronounced "precisely" in Russian, expressing insistence, regret or reflection, and all agreed that this was his unique "way of speech".

P.A. Herzen's return to the land of his fathers coincided with important event for medical specialists—the International Medical Congress held in Moscow.

The rapidly growing class of Russian bourgeoisie had no wish to reconcile itself with life under semi-feudal conditions typical of the tsarist empire. Much more importance was now being attached to human life and the health protection of the well-to-do than ever before, and this promoted advances in the backward public health care system and medicine.

The German pathologist Rudolph Virchow, who also took part in the Congress, and was one of the brilliant minds of his time, made an interesting assessment of the state of Russian medicine. Pathologists usually define the causes of a disease, but, in this instance, the recognized authority in pathology defined the state of public health: "We met youth here which are strong, intelligent, fully prepared for future progress, the hope of this great and glorious nation."

In 1898, having brilliantly defended his thesis, Peter Herzen joined the ranks of a circle of young doctors, the very youth whom Virchow had evaluated so highly—selfless, energetic, well-trained and dedicated to their profession.

Herzen began his surgical career as an intern at the Staro-Yekaterininskaya Hospital (now the Moscow Regional Research

Clinical Institute named after M.F. Vladimirsky) where he worked for 22 years and earned the reputation of an outstanding surgeon of modern times.

At the turn of the century P.A. Herzen revealed his remarkable talent by performing the first successful operation in the world creating an artificial oesophagus. The oesophagus is located deep in the mediastinum, shielded by the thorax, lungs, heart, aorta and other large vessels from the hands of the surgeon.

P.A. Herzen began his medical report with the following statement, rather unusual in style for scientific writing: "The most passionate desire of patients suffering from oesophageal stenosis is to be able to swallow through the mouth." (The phrase reminds one of a few pages from the A.I. Herzen's diary: "...If you probe deeply into life, you will find that the greatest blessing is existence itself, whatever the attending circumstances might be..." Both grandfather and grandson probed deeply into life.)

Peter Herzen delivered his surgical report at the 7th Congress of Russian Surgeons held in December 1907. A quote by Professor P.I. Dyakonov, the famous Russian surgeon who chaired the Congress and edited the journal *Surgery* clarifies for the layman the significance of Herzen's proposal:

"I think that nobody among us will question the fact that the report made by

Dr. Herzen is uncommon and worthy of note, and that Dr. Herzen is a rare talent among Professor César Roux's pupils. This case opens up new horizons for us and we need no longer regard such patients as hopeless."

Soon afterwards Peter Herzen received from abroad a letter sent by his first teacher in surgery:

"My dear colleague! I happened to meet your mother today who gave me your address. I hasten to congratulate you on your splendid accomplishment and am very glad that the pupils are outdoing their teachers. I take this opportunity to wish you well. You must know that all your successes will always be met with sympathy in Lausanne..."

In this instance, however, there were neither vanquished teachers nor victorious pupils. The method of creating an artificial oesophagus out of the intestinal tube became known in the literature as the Roux-Herzen operation. Twenty years later this method was refined by the outstanding Soviet surgeon S.S. Yudin, and became known as the Roux-Herzen-Yudin operation. The chain of names may be extended with those of the group of skilled Soviet surgeons trained by Herzen and Yudin.

To complete the description of this operation and return to Herzen let us quote from another letter included in the book *Vocation* by Professor V.V. Kovanov:

"Dear Peter! I summoned up enough courage to remind you of myself. You have probably forgotten me, but I am alive and well. Many years have passed since your hands shaped the first artificial oesophagus in Russia for me when I was a patient at the Staro-Yekaterininskaya Hospital. I am alive and healthy to this day, the mother of a son who is fifteen years old. I feel fine. My thank to you." The letter was signed: "Saved by you, Yuzefa Sukhornchevskaya, April 10, 1937".

Nothing more need be said, but it might be added that the patient wrote this letter thirty years after her operation. May every surgeon be lucky enough to get such a letter from their patients!

As a surgeon, P.A. Herzen was a true grandson of Iskander, because he boldly tackled any problem, even if it was considered taboo.

Billroth, a scholar of immense authority, warned surgeons that they would lose the respect of their peers if they ever ventured to operate on the heart. A short while after this warning was issued Peter Herzen became one of the first surgeons in Russia to suture a wounded heart and he published his report on the occasion.

"There are two organs in general surgery which are regarded as insurmountable peaks, wrote P.A. Herzen, "they are the heart and the oesophagus. It's high time we mounted an offensive to conquer these fields of surgery." With brilliant operations and scientific articles he prepared to storm these heights.

Herzen was true to patriotism and the legacies of his grandfather throughout his life. When the Russo-Japanese war broke out, M.K. Raikhel, an old and trusted friend of A.I. Herzen and his children, wrote in a letter to her friend:

"...A.I. Herzen's grandson is leaving for Manchuria as a doctor. I have heard that his wife wishes to join him. This is truly an exploit. You probably know that Peter lives in Moscow, at the Yekaterininskaya Hospital, I think. He is among those physicians and surgeons who are being sent by the Moscow Duma Council to the battlefields at Duma's expense..."

When the Great October Socialist Revolution took place, Peter Herzen did not support the old regime. He accepted the revolution heart and soul as a surgeon, scholar, pedagogue, and public figure, participating actively in the construction of the new society.

During the difficult period before the last war Peter Herzen realized that the country would be locked in mortal combat against fascism. Professor I.S. Zhorov, one of his pupils, testified that P.A. Herzen hastened to complete his book *On Haemorrhages*, dedicating it to the Red Army. The work proved to be of invaluable assistance to surgeons at the front during the Great Patriotic War.

Herzen, the true patriot, declared: "We must not only advance science, we must be able to shoot!" The elderly professor joined a sharpshooter circle organized at the Medical Institute and began training in marksmanship.

Herzen's real weapon, however, with which he was unsurpassed in skill, was the scalpel. His pupils were unanimous in opinion that apart from all other aspects of the profession, the operations he performed were accomplished with consummate beauty. Could this also have been an allusion to the grace of his fingers (incidentally, he was also an accomplished musician). The beauty of operating as seen by a specialist in surgery embodies a thorough knowledge of anatomy, a keen understanding of the disease, an absence of fuss, precision of movement, calmness and assurance and the ability to wield the scalpel to terminate the pathological process.

P.A. Herzen was both temperamental and expansive in nature, but he never lost self-control. It was hard to judge how things were going on the operating table because of his composure. It was only afterwards that it became clear what hazards had been avoided due to the skill of the surgeon.

Such freedom and ease in performing the most complex of operations is the result of knowledge and experience. "The surgeon has no right to use a scalpel," Herzen strictly warned, "unless he knows anatomy, the possible physiological complications and their causes."

Peter Herzen possessed a fortunate combination of all this knowledge. Both his doctor's theses (the first written in Lausanne and the second, in Moscow) were clearly oriented towards pathophysiology, while his training in anatomy allowed him to win, unrivalled, an appointment in 1919 to the Chair of Topographical Anatomy and Operative Surgery at the Medical Faculty of Moscow University.

Here again, one cannot but note the remarkable coincidence in the philosophical approach to the treatment of patients by both Iskander and his grandson. In a favourable recommendation written for Doctor M.V. Rikhter, A.I. Herzen emphasized that he studies every patient with careful consideration, "as a fact of science". Peter Herzen also advised every operation to be handled as a unique scientific experiment; in other words, the surgeon should not only operate, but also analyse the post-operative phenomena so as to be able to retreat in good time if he begins treading on false ground. He claimed that in contrast to an experimental physiologist, the explorations of a surgeon must always be in the interests of the patient.

Although he recognized the importance of the scientific foundations in surgery (anatomy, physiology), Peter Herzen assigned a considerable role to the personal qualities of the operating surgeon, to his intuition and temperament, because he believed that success is impossible without inspiration.

Herzen was a tireless worker. He invariably echoed his famous grandfather in proclaiming: "Hard work is our prayer!" At the Moscow Oncological Institute which was named after him, operation journals are filed that serve as documents of day-to-day work. Opening one of these diaries at any page, we find the following entries: operated a brain tumour, carcinoma of the mammary gland, the tongue and the stomach. It lists the surgical interventions characterizing the range of his abilities, as well as his amazing industriousness.

According to his own count, by the 25th anniversary since the beginning of his surgical practice (and that was only just the middle of his career!) Herzen had personally performed 12 000 serious operations. He had every right to say, "Not a single day without work!" Even if we calculate a rate without excluding Sundays and holidays, leaves, sick days and business trips, on the average he performed 1-2 operations every day.

It was an astounding surgeon and remarkable personality that became head of the Moscow Oncological Institute in 1922. But before we describe P.A. Herzen's work at this post we must describe the state of oncological health services in Russia at the time.

Men Against Cancer

No specialized institutions for the treatment of oncological patients existed until the end of the last century. Knowing no radical means for combatting the disease, medical specialists were more concerned with charity and relief for the sick. One of the appeals drawn up by Moscow surgeons L.L. Levshin and V.M. Zykov spoke of the tragic state of the people who suffered from cancer:

"If we could picture our tremendous country we would see what great numbers of people are now battling with this terrible disease, enduring indescribable suffering."

Having drawn a hopeless picture of oncological aid and of the desire of most patients to seek treatment in Moscow, the authors of the appeal stressed that there was nothing in Moscow either to help them.

On November 18, 1903, the first institute in Russia, and one of the first in the world for the treatment of patients with tumours, was founded exclusively financed by private donations. This is now the Herzen Oncological Institute in Moscow. At the time it was a special building containing 56 cots (approximately 100 patients could be admitted there). The institute was located on Malaya Pirogovskaya Street in Moscow.

Recollections of contemporaries about Professor L.L. Levshin, the first director of the institute, were not preserved for history; however, the authors of this book were overjoyed to come across his name among the letters of Maria Chekhova. Apparently, in 1898 Levshin operated on Chekhov's 74-year-old father for a strangulated hernia. The injury occurred at the country house in Melikhovo when nobody was at home. Much time passed before the patient could be delivered to Moscow. Necrosis set in and a length of the intestine had to be removed.

This is how Maria Chekhova described her meeting with Dr. Levshin immediately after the operation: "The doctor was exhausted, his hair stuck to his head and his hands were covered with blood. I told the doctor that I had left father in a healthy condition and that the telegram had caught me by surprise. He expressed sympathy and informed me that the operation had been quite successful, and that I would even be allowed to hear father speak. I was taken upstairs where the blood-stained attendants stood around father, shielding him from my view, but I heard his voice which was quite strong..."

It is interesting to note that the doctor attending Chekhov's father was Zykov, who had been Levshin's assistant at the time and who eventually became the second director of the Oncological Institute.

Maria Chekhova continued in her letter: "I left the clinic only to return the next morning. They said that Dr. Zykov had spent the night by father's bedside but was now sleeping, just as his patient. We waited for the professor, who proved to be a very pleasant man, and were invited to his private office. I stayed there for a few hours speaking to the physicians while father slept. He only awoke at one o'clock and we were informed that his pulse and temperature were normal. Doctor Zykov escorted us to him and father told us in a weak voice that he had been unconscious of the operation. We left and Zykov asked me to come again in the evening, when I found father feeling much better. He is being taken care of very well. He asked mother to visit him and spoke of the doctors whom he held in high regard..."

As is known, Pavel Chekhov did not survive the operation and died suddenly from thromboembolism of the pulmonary artery, a complication not connected with faulty surgery.

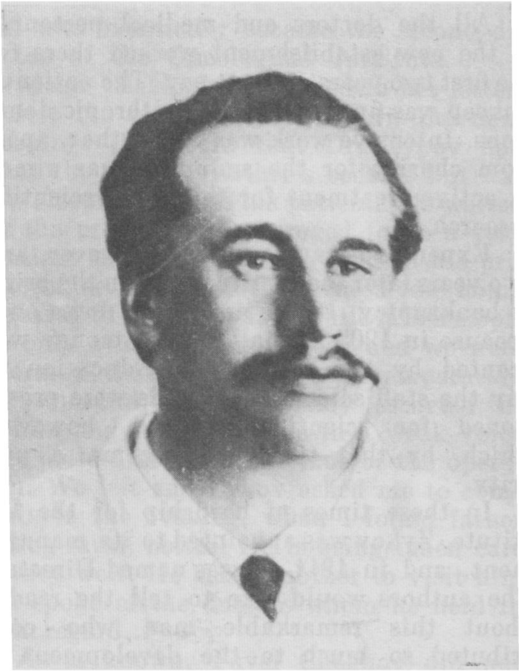
This excerpt describes Levshin not only as a skilled surgeon who proved to be bold enough to assume responsibility for a serious abdominal operation in an elderly man, but as a kind and sensitive person who created an atmosphere of goodwill in the clinic and later at the Oncological Institute.

All the doctors and medical personnel of the new establishment worked there for the first two years without pay. The patients' upkeep was financed by philanthropic donations. Intensive work was begun that, apart from charity for the suffering, was aimed at active treatment for them and scientific research.

Expenses began to mount, however, and two years later the Institute was on the brink of bankruptcy. It was not closed down only because in 1905 a small sum of money was granted by the Ministry of Education to pay the staff salaries. No funds were provisioned for scientific research, however, which by that time had become a priority.

In these times of hardship for the Institute, Zykov was appointed to its management, and in 1911 he was named Director. The authors would like to tell the reader about this remarkable man who contributed so much to the development of oncology in Russia.

Zykov's father was a painter who had bought his freedom from serfdom. Orphaned at an early age, Vladimir Zykov made his way through life on his own. He graduated from the Medical Faculty of Moscow University, studied languages and, within a short period of time, became recognized as one of the best surgeons in Moscow. He was the first in the country to perform radical operations for carcinoma of the mammary gland



V.M. ZYKOV

and one of the first to use surgery for cancer of the stomach.

When he transferred to the Oncological Institute, Zykov gave up his high university salary and was obliged to move with his wife and three children from his excellent professor's flat to a small wooden house located on the Institute's campus near the students' dormitory. It was mentioned above that during the first two years Zykov and the other physicians worked without pay. Nuns from the nearby Devichye Monastery worked as nurses and hospital attendants.

These were the roots of Russian oncology.

By 1913, which marked the tenth anniversary of the founding of the Institute, the cornerstones of theoretical science and clinical practice had been laid. A wide search was carried on for specific anti-tumoral agents. Not only the scalpel was used in treatment, but also a variety of chemical substances and enzymes. Here, the foundations for Russian radiology were laid.

According to official records, 50 mg of the precious substance was purchased for the money received from the sale of the Institute's collection of scientific works in the anniversary year of 1913. But radium therapy had already been mentioned in the articles published by the Institute as far back as 1905.

A.V. Talalayeva, D.Sc. (Med.), the granddaughter of Zykov, informed the authors of this book that, according to family legend, the first radium had been a gift of the world-famous physicists Marie and Pierre Curie, who were immensely impressed by the efforts and the results produced by Russian oncologists.

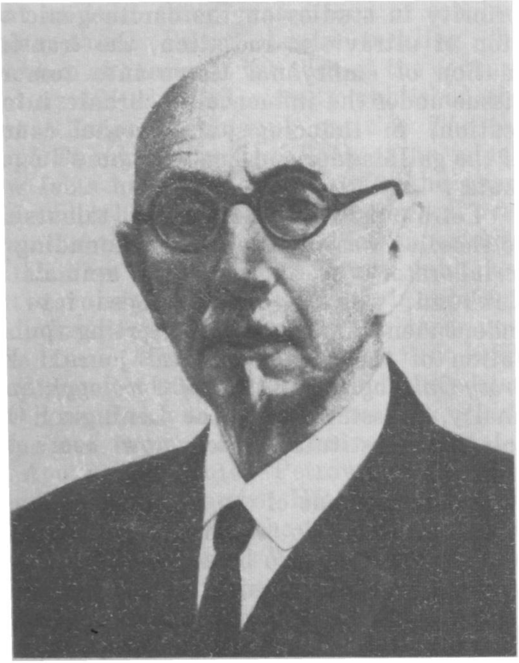
The Institute was among the first oncological establishments of the time to treat malignant neoplasms. Investigations of the mechanisms governing tumoral growth had overtaken in many aspects of the problem the level of scientific understanding in other countries.

Zykov proposed that one of the causes of malignant tumours is a disturbance of the respiratory processes. Based on this concept, the Institute began an active study of the oxidation reactions in tumours and in the organism of patients. V.M. Zykov, D.V. Nenyukov, M.A. Tsukerman and V.A. Bogorodsky were the first in the world to establish that there is a reduction in the oxidation processes in the tissues of cancerous tumours. These data were obtained 12 years before publication of Warburg's well-known research that was later awarded the Nobel prize.

At this Institute, V.K. Vasiliev was the first in Russia to grow cells of malignant neoplasms from animals and men outside of the organism. His results were published in 1913, just a year after Carrel reported his new method for the explantation of cells.

Apart from their routine work, the staff of the Institute widely distributed information about cancer prevention and explained why it was necessary to detect its symptoms as early as possible; they delivered lectures to students, physicians, doctors' assistants and midwives.

Meanwhile oncological institutes were being opened in many European countries.



N.N. PETROV

In St. Petersburg, Nikolai Petrov was becoming more and more active. The name of this scientist opens up an epoch in the history of Russian oncology. If we were to simply enumerate all his achievements and interests, the reader might think that this was not one man, but a group of scholars.

In experimental oncology Petrov has

priority in studies on the carcinogenic action of ultraviolet radiation, the transformation of embryonal tissue into tumoral tissue under the influence of chronic intoxication, in inducing experimental cancer of the gallbladder and bone tumours in primates.

Petrov had organizational talents in science, as was revealed in his founding of a laboratory of experimental animals in Sukhumi, which later developed into an independent institute, in starting publication of the Soviet medical journal *Voprosy Onkologii* (*Questions of Oncology*), and, finally, in establishing the Leningrad Oncological Institute, which now bears his name.

Petrov was one of the initiators of mass-scale prophylactic examinations in this country. It must also be added that he contributed much to refining methods of diagnosing and treating oncological patients. He himself was an excellent surgeon, and an observant, sensitive, and kind physician. It is no wonder that he is recognized as the founder of deontology, a science establishing the standards for a doctor's behaviour in caring for patients. His extensive work in popularizing medical knowledge for the prevention of cancer, his work in military field surgery and in many other educational areas has not even been mentioned.

Examining the chronology of Petrov's scientific publications, one might think that at least three generations of scholars wrote them. Petrov began tackling the problem of cancer at the turn of the century and by 1910 he had already published the first Russian monograph entitled *The General Theory of Tumours*, a book to which new facts have been added over the years and which has been published over and over again, retaining its scientific importance to this day. In the thirties Petrov published a two-volume guide to clinical oncology and, in the post-war years, the three-volume book *Malignant Tumours*. In 1958, 48 years after his first monograph, he edited the book *Guide to General Oncology*, which came out in several successive editions.

Age never tainted Petrov's inquisitive mind or active nature. His working capacity seemed to be inexhaustive. During the last 10-15 years of his life, when he was already well along in years, Petrov spent his summer vacations in Ostashkov, a town on the shores of Lake Seliger. Doctor G.L. Tsyrulnik, a long-time resident of this town, recalled that when Petrov began to spend his summer vacations there, all the surgeons of the local hospital stopped leaving town for their summer vacations. Every morning the elderly Academician would bicycle to the hospital, don a white smock and join the physicians on their rounds, helping with consultations and operations, never for a moment away from his favourite occupation—teaching doctors and treating patients.

The cancer offensive against human lives in the latter half of the twentieth century was no surprise for medical specialists. As was mentioned, preparation for it had begun at the turn of the century although they were disrupted by World War One in 1914. Because of the war, the Moscow Oncological Institute was converted into a hospital for the wounded and later for people stricken by typhus. It was only in 1920 that the establishment was reopened for patients with malignant tumours.

In 1922, Peter Herzen became the director. Herzen proved to be more than a lucky choice for a number of reasons, among which his firm political belief as a direct descendent of the Great Democrat was far from the least of them. During those difficult revolutionary times when some of the intelligentsia were confused and uncertain whom to side with, and sometimes even resorted to open sabotage, Peter Herzen resolutely upheld the red banner and, basing his Surgical Faculty at the Military Communist Hospital, began treating soldiers and commanders of Red Army. His popular name rallied many young physicians and researchers to the Oncological Institute.

Herzen's appointment to head the Institute was also lucky because he was an outstanding surgeon who could operate with immense skill on all organs of the body. It must be borne in mind that in the twenties radiation therapy was only in its early stages of development and nothing was known about drugs for the treatment of malignant tumours. Surgery represented the only hope for curing cancer. As director, P.A. Herzen immediately increased the capacity for surgical intervention at the Institute by almost three times, and, through his own research, sought to refine the techniques.

An eminent clinician and surgeon, Peter Herzen had developed a liking for physiological and biochemical research from early youth (it should be recalled that his father was a prominent pathophysiologist and that both of Herzen's theses for the medical degree were oriented in the same field). This is why experimental and theoretical research found such favourable ground for development at the Institute. Moreover, it should be added that in character Peter Herzen was an unfailing optimist (a trait no less essential for specialists in oncology today).

The opinion prevails that Herzen founded the Moscow school of oncology, while Petrov was the father of the Leningrad school. Such a division is more geographical than scientific. Both scientists laid the theoretical, clinical and organizational foundations of modern oncology. When one reads their works, one is amazed at their scientific foresight and intuition. Herzen's report entitled *An Introduction to the Clinical Treatment of Surgical Forms of Cancer*, which he delivered more than half a century ago (April, 1930) at a Conference on Cancer Prevention held in Moscow, illustrates the point. The programme he outlined in his report is topical to this day.

A philosophical approach to facts was very typical of Herzen (no doubt he received phylosophical training still at home). Thus, grounding his thinking on the vast amount of his own clinical observations, he discerned the general pattern of cancer development in different organs, and from these common features tried to determine the cause for the development of malignant tumours, and to outline preventive measures.

What are these common features?

Advanced or old age is one of the first features. Peter Herzen emphasized that the tumour most often "prefers" an altered environment. In occupational cancer of the skin, for example, and as has been demonstrated in experiments on animals, malignant growth is preceded for quite a while by non-cancerous changes. In exactly the same way a chronic ulcer of the stomach may develop into carcinoma. (Due to his inherently outspoken nature Herzen called the clinicians who failed to notice this "blind men".) Herzen expressed quite contemporary opinions regarding the causes of carcinoma of the mammary gland, emphasizing the significance of hormonal disorders caused by abortion, the premature cessation of breast-feeding, etc.

It proved impossible to define the moment when an ordinary cell turns into a tumour cell (to date nobody has succeeded in this!). Peter Herzen explained that due to the influence of carcinogenic agents, a gradual accumulation of quantitative changes takes place which leads to a qualitative leap, i. e. the appearance of transformed cells.

Based on the facts enumerated above, Herzen advanced a thesis regarding the role of external factors in carcinogenesis, although he immediately forewarned that these factors alone are insufficient, because "... under equal external conditions, one person may contract the disease, while another will not; one may become ill quickly, while another becomes ill much later..." Moreover, different forms of cancer can mature in one and the same organ. Herzen was one of the first to perceive that the biological characteristics of the tumour depend on its morphological structure. For example, a carcinoma distinguished by more differentiated cells, develops less fiercely (if this word can be applied to malignant growth). In the same way, P.A. Herzen drew conclusion about the role of internal, endogenous factors in the development of malignant tumours. According to him, these include disorders of intracellular metabolism and the hereditary factor. Here Herzen correctly points out that it is not cancer which is inherited, but the predisposition to cancer.

Although Herzen's report is entitled *An Introduction to the Clinical Treatment of Surgical Forms of Cancer*, it raises vital problems of theoretical and clinical oncology, and, in essence, presents the credo of the head of the Moscow school.

Regarding diagnostic and therapeutic approaches, Herzen categorically objected to keeping a patient under observation for months on end until the suspected malignant tumour becomes palpable: good treatment results may only be achieved through early diagnosis. This reminds one of the basic principle to which the Herzen Institute adheres to this day: research is now mainly oriented towards studying the problem of early stages of cancer in all its aspects—morphology, diagnostics and treatment.

Herzen never operated on oncological patients according to a simplified scheme as some, even prominent, surgeons did, who tried to suit their actions to the case before them as to a Procrustean bed of acknowledged rules. Some advocated that a small tumour calls for a big operation, or, if the disease had been neglected, limited surgery. Others (who could be labelled "superradicals"), asserted that a small carcinoma called for a big operation, and a large carcinoma justified an even bigger operation.

Herzen stated that discussions about treating cancer in general were pure abstraction; there exists a scheme that permits deviations from it justified by the specific features of both the tumour and of the patient's organism.

He was one of the first medical specialists in the world to express a common sense approach, namely, that there are limits to the surgical treatment of every tumour within which it can be radically removed. The less the tumour, the narrower these limits. This reveals another connection to current practice, when organ-preserving operations for cancer are gradually departing from casuistry to become the rule.

In asserting his credo Herzen insisted that, in the fight against the cruel disease called cancer, increasing the oncological literacy of physicians and improving the sanitary culture of the population are of essential importance. He emphasized that cancer prevention is impossible without the active participation of the state government.

It was greatly due to Herzen's activities, to his enthusiasm, energy and knowledge, that within a comparatively short span of time the Institute became the centre for cancer treatment in the country and developed into a prestigious scientific research establishment pioneering investigations of the basic problems in theoretical and clinical oncology.

In 1931, just ten years after the Civil War came to an end, the First All-Russia

Congress of Oncologists was convened, and three years later the government of the Russian Federal Republic published a decree entitled "On Organizing Measures of Cancer Prevention" on the basis of which medical stations specializing in oncology were set up in 52 regional and territorial towns of the country. Finally, in 1938 the USSR Anti-Cancer Committee was organized headed by Professor A.I. Savitsky. The purpose of this Committee lay in organizing anti-cancer measures, standardizing registration of the incidence and mortality from malignant tumours, and coordinating scientific research in the field of oncology.

Alexander Savitsky was Herzen's closest assistant. The authors of this book had the fortune to know him personally, to converse with him, to listen to his lectures and to accompany him on patient rounds. He belonged to the brilliant group of students studying under Professor A.V. Martynov, after whose death the direction of the Moscow University Clinic passed on to P.A. Herzen. Martynov's young assistant, Savitsky, rapidly became a leading figure at the clinic. Soon after he went to work at the Oncological Institute and in 1944 was appointed its director.

Savitsky was one of the first specialists in the country to perform surgery on the lungs. His powers of observation and sound logic made him a prominent diagnostician,

A.I. SAVITSKY

But Savitsky revealed an even greater talent in organizing measures of cancer prevention.

Certainly, the victory over diseases occurring on a mass scale begins with the organization of measures to prevent them. The case of tuberculosis and malaria are examples of this success.

As was mentioned earlier, there was a time when consumption caused death on a large scale and aroused so much concern that it overshadowed oncological diseases. Tuberculosis was cured only by the creation of a network of anti-tuberculosis dispensary posts.

Malaria was also rampant at one time. In 1938 the number of victims it claimed throughout the world reached 170 million with approximately 3.5 million people dying every year. It proved to be more disastrous than the plague and cholera combined! In the Soviet Union 660 anti-malaria stations were organized while the number of anti-malaria posts was doubled. The vigorous anti-malaria measures taken in the prewar years produced impressive results: instead of the 10 million patients registered in prerevolutionary Russia, in 1938 their number was reduced to between 1.5 and 2 million, and today only random cases occur.

In April, 1945 when the echoes of the Great Patriotic War had not yet died down, many wounds were waiting to be healed, and the country was faced with the tasks of reconstructing demolished towns and villages, the USSR Council of Peoples Commissars passed a special resolution "On measures for improving oncological aid to the population" that was aimed at increasing the number of anti-cancer dispensary posts, the number of beds in oncological hospitals, etc. It was symbolic that in many regional towns hospitals were converted into oncological dispensary establishments. Considering this turn of events, a short digression into the area of field medicine is appropriate.

One of the reasons for the Soviet Union's victory over fascism was the return of wounded back to the ranks of fighters, which was unprecedented in the history of wars. Even in the severest first period of the war, when the troops were retreating in battle and the country which had lost its main economic territories was suffering crippling losses and difficulties, healing of the wounded far surpassed that of the enemy's armies although Hitler's troops were better equipped in terms of transport and medical supplies, and German surgeons were traditionally considered the most skilled and experienced in Europe. Why then was this so? The crux of the matter lay in organizational principles, in the military medical doctrine.

The Russian, and later the Soviet, warfield doctrine had been developing for decades, starting with the Crimean War. The brilliant surgeon Nikolai Pirogov stood at its source. The essence of this doctrine lay in sorting out and evacuating the wounded according to their condition, as well as in locating skilled medical aid in maximum possible proximity to the troops in battle.

For example, it is known that the chances of recovery from an abdomen wound are far greater if the required operation is performed within the first six hours. Any delay means death. This is why men wounded in the abdomen were separated at the regimental-medical post, i.e., within a kilometre from the battlefield, and they were given priority in evacuation to the nearest medical corps battalion (no more than 6-7 kilometres) where a special team exclusively performed such operations.

One of the authors of this book served as part of such a team during the war and shall never forget the sleepless hours on duty working under fire in either a tent or a dugout for 16 to 18 hours at the operating table. As soon as the condition of the wounded man and the battle conditions permitted, the patient was shipped on specially equipped buses or aircraft to specialized hospitals, where he could be attended to more calmly and with greater care. The same principle was adhered to in tending to other kinds of wounds.

The German field hospital and medical doctrine was adapted to the "blitzkrieg" theory. As long as this theory was applicable the wounded did not suffer. During the battles in Flanders and France practically all the soldiers who were seriously wounded were immediately flown to big hospitals and clinics in central Germany. Return to the ranks was very high.

All this changed drastically when the fascists attacked the USSR. The "blitzkrieg" mode of war was completely upset by the brave resistance of the Soviet people. The end of the war seemed farther and farther away, communications were strained and the number of wounded grew so rapidly that transportation did not suffice. It proved impossible to deliver patients to the operating tables in the far rear. The enemy was obliged to hastily reorganize their military medical service, but the losses grew not only because of the greater number of wounded, but also because of delayed skilled medical aid.

Thus the Soviet military medical doctrine prevailed over the German system and became one of the factors in the great victory over the fascists.

It would seem that there is no connection between this digression and the topic of this book; however, the connection is a very close one. To cope with any widely spread disease among a population, there must be a code of principles, laws and provisions, i.e., a specific scientifically grounded doctrine. Without this, anti-cancer measures can also yield no positive results.

Apart from the minor details, the oncological doctrine is made up of two equally important components: detection in good time, and treatment appropriately chosen to fit the specific characteristics of the tumour and the patient's organism. However, the doctrine alone, without a corresponding system to provide for it, is empty talk.

Taking into account the importance and urgency of the problem of preventing malignant neoplasms, the USSR Council of Ministers adopted a decision in April 1976 to further expand and strengthen the network of oncological institutes. Special attention was focussed on establishing big multiprofile dispensary clinics equipped with modern diagnostic instruments, powerful gamma-therapeutic installations and equipment for performing the most sophisticated surgical operations.

The Soviet Union now boasts an efficient system for providing aid to oncological patients which has no equal. This service is headed by the Board of Oncology of the USSR Ministry of Public Health. Scientific research is coordinated and directed by the Scientific Council for Malignant Neoplasms of the USSR Academy of Medical Sciences. Academician N.N. Blokhin, Chairman of this Council, is also in charge of the Oncological Scientific Centre of the AMS of the USSR, which is staffed by outstanding scientists of world renown. The departments and laboratories of the N.N. Petrov Oncological Institute headed by N.P. Napalkov, Academician of the AMS of the USSR, are housed in several new buildings in Leningrad. Each of the Union Republics has its own centre for the consultation and treatment of oncological

N.N. BLOKHIN

patients, represented by the scientific research institute of the Republic. Special departments in these institutes organize and control the activities of smaller oncological centres in outlying districts.

Oncological dispensary clinics have been set up in most regional and territorial centres. Moreover, in such big cities as Moscow, Leningrad, Sverdlovsk, and Saratov there are also municipal dispensary clinics. They are subdivided into polyclinics, in-patient hospitals and methodological departments. Many of the large dispensary clinics also function as teaching hospitals for medical colleges, where specialists are trained.

In recent years society has been tackling the problem of returning the working capacity and social potential to oncological patients. It is most essential to restore not only the physical ability to work in such people, but also to bring peace to these deeply traumatized human beings. Not only oncologists, but also psychologists, sociologists, economists and representatives of social security departments take part in solving the problems of rehabilitation. It should be emphasized that the return of many thousands of people who have been ill with cancer back to a normal healthy life does not only have an immeasurable moral significance, but also promises society great economic advantages.

There are now 21 oncological and roentgenoradiological institutes in the USSR, 248 oncological dispensary clinics, 3376 oncological departments and offices, and nearly 55 000 beds at in-patient clinics for those stricken with cancer.

The socialist countries widely apply the organizational principles underlying the foundations of the Soviet oncological health service, but they do not copy the experience, preferring instead to elaborate on it creatively in accordance with their own medical traditions, state, geographical and other specific features. In the West a proper anti-cancer prevention system is hampered by defects in their general system of public health.

The well-known French oncologist Professor P.V. Denois, formerly the Assistant Minister of Public Health, once told the authors of this book that considerable difficulties in his country arise due to the fact that health establishments are either state or privately owned. Many physicians with private practices have their own offices for radiation therapy and sometimes prescribe such treatment more frequently than is required. This violates the principle of combining several treatment methods (surgical, radiation, drug therapy and others), which is necessary for the treatment of certain forms of cancer.

In Great Britain there are only three specialized oncological centres and patients are often obliged to seek treatment at general hospitals that are poorly equipped.

The World Health Organization (WHO) has demonstrated an interest in oncology from the time of its establishment. It is worthy of note that in the first ten years after the World War Two the problem of oncological disease was listed only sixth in importance for mankind, and only after 1958 was it granted priority on a level with cardiovascular diseases.

According to the data collected by the well-known Soviet oncologist Professor A.M. Garin, who headed the Oncology Department of WHO in Geneva, in most of the developed countries approximately 9 per cent of the budget allocations for public health are spent on aid and services for oncological patients.

The ever-increasing flow of scientific publications, numbering tens of thousands of articles every year, indirectly testifies to the burgeoning scale of the search for the causes of malignant tumours, methods of cancer prevention, diagnostics and treatment.

To rid mankind of cancer, it is urgently necessary to unite the efforts of all researchers in the world. This is the purpose of the International Union Against Cancer in which Soviet oncologists take a very active part.

The USSR is a member of the International Agency for Research on Cancer which has its headquarters in Lyons. Moreover, the oncologists of the socialist countries have elaborated a wide joint programme within the framework of the Council for Mutual Economic Aid. On the basis of various intergovernmental agreements between the USSR and some of the Western Countries, coordinated programmes have been worked out dealing with certain problems in oncology. The joint efforts of all scientists will undoubtedly hasten the day when a victory over malignant tumours can finally be declared.

Academician Nikolai Blokhin, the eminent Soviet oncologist, said, "Cancer is often called the disease of the 20th century because it is in this century that conditions were created that gave prominence to the problem of oncology, but at the same time the 20th century provides particularly favourable conditions for tackling this immensely complex problem."

Legends About Cancer

Medical legends, that is, non-scientific, unverifiable stories about diseases, their causes and methods of treatment are encountered all the time. This can be explained by the ambiguous character of medicine, which appears to be a complex blending of science and art, of seemingly accessible medical knowledge and the acute interest of people in preserving their health and the health of their loved ones.

Many people, probably, still remember the widespread legend of the seventies which held that a treatment course of subcutaneous injections of novocain was a sure method for returning youth. As it turned out, the temporary positive effect produced in some people was due to all the attendant circumstances of such novocain treatment, namely, the necessary stay in a quiet hospital, vitamin therapy, hygienic measures and so on.

Similar hopes are fostered in some credulous people by the current sensation of "extrasensory" powers, which are allegedly capable of making a diagnosis and treating patients by means of a hypothetical "biological field".

In an article entitled "True or False? Can It be Distinguished?" Academician

A.B. Migdal stated his view: "It is possible to suppose the existence of yet undiscovered physical fields. In the sphere of energies and frequencies, all the fields which produce an effect on physical instruments have been exhaustively studied. If an electron moving in an accelerator were affected by some unknown field, its motion would differ from the calculated path, but this has not been registered by experiment. The probability of discovering a new type of physical field on the macroscopic level is so slight, that one can hardly consider."

But couldn't there be some kind of *non-physical* forms of energy, emitted and received by living beings, which make such "miracles" as telepathy possible, for example? Couldn't there be a special kind of biofield around organisms?

Migdal proves very clearly that this contradicts the data of modern biophysics and emphasizes that no manifestations of a biofield that have been confirmed by scientific experiment have been detected.

The myth of a "biological field" cannot be proved. But some people believe in it as they believe in God.

One such myth was created recently by the American philosopher Dr. R. Moody, the author of *Life after Life*, subtitled, "The Investigation of a Phenomenon—Survival of Bodily Death".

A slight correction should be made: we attributed the myth to the above author, but this is incorrect. The legend of life after death is as old as the Earth and Moody only tried to substantiate it with vestiges of science. He merely systematically presented the impressions he had collected of people who claimed "to have been in the other world" and who were brought back to life by the efforts of medical specialists.

The scientific level of this book may be judged by the passage where Moody describes the transition into the other world. The person realizes that he possesses a body but of quite a different nature and with absolutely different properties than that physical body which he had abandoned... He is welcomed by the souls of relatives and friends who have already died and is confronted by a luminous being which exudes such love and soulful warmth which he had never experienced...

At some moment, however, the man senses that he is being called back, that his hour of reckoning has not come yet.

At that point he begins to resist, because now he knows what the other life is like and does not want to return. He is brimming with feelings of joy, love and peace, despite his resistance he is nevertheless somehow reunited with his physical body and thus returned to life...

It is doubtful that such a narrative requires serious critical analysis. It is quite possible that some people who had been resuscitated dreamed something up. Moody fails to provide any convincing evidence that the patients he questioned had really experienced the state of clinical death and not a common fainting spell which is often accompanied by acoustic and visual hallucinations. It is also possible that such beautiful dreams resulted from taking drugs, in particular, LSD.

The message of Moody's treatise is more than clear: fear not life beyond the grave, because life in the "valley of death" is not so grim after all. "Oh! I died! How wonderful!" exclaims one of Moody's subjects. Here is the reaction of still another woman (if one can believe Moody). After she returned to this world she wept a whole week because she is obliged to live in this world again after seeing the other. To make such a confession one must either be abnormal or desperately overburdened by the daily troubles of life.

The considerable experience that the authors of this book have had in medicine and with patients reveals that those who have recovered after a severe disease or operation when they were between life and death are actually apt to be overcome with incredible joy, even euphoria, from the "gift of health" they have received.

Regarding what is remembered by patients whose clinical death had been medically documented (the authors have personally encountered only a very few such cases), they never knew that at some instance the physicians themselves were not sure whether their patients were nearer to life or to death. Of course, nobody ever told them about this.

...No disease has ever sprung as many tales as cancer. The fear of cancer can only be compared with the reaction of panic in past centuries to leprosy. It is no wonder that the answer to the question, "What discovery that could be made before the advent of 2000 A.D. would be greeted as the greatest blessing by all people?", given by the overwhelming majority of the population of the United States and some European countries was "a solution to the problem of cancer". It is therefore not in the least surprising that to this day sensational reports regarding the fantastic possibilities of anti-cancer measures are readily greeted with childish credulity.

At the beginning of the 1970s a book by the professor of theology Ivan Illich, entitled *Medical Nemesis*, caused quite a commotion in the West. The author was biased on choosing cases where there were complications following treatment, and in speculating on the limited possibilities of medicine in curing some diseases to formulate the opinion that physicians not only fail to help patients in serious cases, but often cause harm because they are allegedly to blame for various new diseases afflicting their patients, ranging from drug addiction to psychological disorders. According to Illich, for example, the attempt to use ineffective means to treat incurable diseases (primarily cancer, of course) is a fine illustration of his point. If the hopelessly ill patient had not known his diagnosis, he would have felt well enough to live out two-thirds of his remaining life.

Groundless and incompetent judgements about the successes and failures of medicine are no novelty. People have long been evaluating the work of physicians without the slightest idea of what medicine can or cannot do. Russian history tells of a legend when a German physician named Anton treated a prince by the name of Karakucha. As a result of this treatment the sick prince died, whereupon Ivan the Third, the Grand Duke, ordered the doctor to be butchered like an animal in retribution.

In our times, of course, no one is punished in this way for failing to cure a sick person, but severe punishment for causing death by inept treatment is meted out often.

What has been narrated may be explained in two ways: either there is a blind faith in medicine being all-powerful, or, on the contrary, complete skepticims, a desire to let illness take its own "natural" course, or irregardless of the consequences, find a magician who possesses special healing powers. All these approaches reflect a lack of information about the contemporary level of knowledge.

V.V. Veresayev, who practised medicine at the turn of the 19th century, expressed frustration at the limitation he experienced as a physician:

"I can no longer tolerate the anguish people cause me every hour, every day... The fact that I penetrated the essence of nature just a little deeper than others makes people think that, like a god, I am capable of delivering them from suffering and of granting happiness, but I am only a human being just as they are. If you could only know what anguish I experience and how my heart practically comes to a stop when, instead of saving a sick person, I can only utter a few words of consolation to people who are dying. What awaits me? A man surrounded by universal esteem, but actually a plain, helpless human being?"

In our times there cannot be such a feeling of helplessness. Physicians succeed in saving a tremendous number of patients who just 20 years ago would have been doomed. We are justly proud of the achievements of medicine in general, and of oncology in particular. Confirmation of this is the consistently increasing number of people who have undergone radical treatment for their malignant tumours and have survived after their operations for five years and more. According to the data collected by Academician N.P. Napalkov and his assistants, the number of former patients registered by oncologists in our country alone is nearing one million.

There are some novelists who supercharge their stories with an atmosphere of "cancer hopelessness". With amazing stubbornness some writers keep drumming into the heads of their readers that malignant tumours are incurable, arousing a mystic horror in their minds. Lev Tolstoi can be forgiven for this, because at the turn of the century nobody could actually cure cancer; at the same time victory over most infectious diseases, syphilis, leprosy and others was just as rare. A. Grin, the Soviet romantic writer, can also be forgiven because he used cancer to provide a background for the inner drama and death of his otherwise fortunate and courageous hero. But modern writers should not be forgiven.

The writer can doubtlessly find much in the psychology of a cancer patient to characterize dramatic moments in life, but he has no right to present these facts in the most gloomy, and even sometimes false, light, disorienting the reader.We can only wonder why writers have never presented a hero who suffered the shock and torment of being stricken by cancer and who recovered and returned to active life.

If a person suffers from heart trouble, he usually makes no tragedy of the fact, but if he has a malignant tumour he considers himself doomed. To a great extent this is due to the way in which a person dies: in the former case, as a rule, his death occurs suddenly and almost without pain; in the latter case, death is a slow and torturous process, creating a very distressing sight. The fear of death from a certain disease is transferred to the disease itself. In his story *The Sentence* author V. Soloukhin proclaims a rather strange toast: "Let's drink to cardiovascular disease! Although it already claims priority in the world, we must drink to it nevertheless, because if we choose the one which is in second place..."

In the novel *Kontuzja* by the Polish author Z. Bystrzycka, the heroine of the novel has seen cancer as "lurking during life decaying organ after organ; that is why myocardial infarction or diabetes mellitus are called clean whereas cancer is considered a dirty disease".

It is no wonder that a person becomes so frightened that he gives up without a fight, and that the disease is unambiguously equated with death! At time the characters in stories or novels are shown debating with themselves whether to turn to a doctor on feeling sick or to let nature take its course and simply hope for the best.

In the story *The Sentence* mentioned above, there is a description of the case history of the hero; an episode is described where he meets a person who had a similar pigmentary tumour: "In the hollow of his chest," wrote the author, "there was a flat black patch, compared to which mine, which was the size of a pea, was like a chicken next to a turkey. It was like a medium-sized coin with smaller beans surrounding it."

"How long have you had it?" I exclaimed.

"Eighteen years now," he replied. "It has been there for fifteen years remaining the size of a pea without growing. In the last three years, it has been getting bigger. I think I'll last another five years, no more."

Thus, 18 plus 5 makes 23. Such is the fate of man "who took off from a dangerous shore, because nobody can live so long after an operation. If he survives, it means the tumour was non-malignant. After an operation people often die within a few months and few—about 10 per cent—survive beyond three years. So it's up to you: either go ashore where there are cannibals and crocodiles, or sail out into the sea again..."

This story, just as others written by Soloukhin, rings with true sincerity. This is why the hero's reasoning in regard to the medical aspects of the disease are accepted by most readers as factual. There have been people who were themselves suffering from malignant pigmentary tumours and even refused to be operated on after reading the book. Let us analyze this excerpt from the point of view of oncology specialists.

Proliferation (spreading of the process) after removal of malignant skin tumours is possible under two conditions; if it is removed non-professionally (e.g., by tying a thread or economically, cutting too close to the tumoral tissue); and if the spread of the tumour cells (metastases) occurred already before the operation but had not become manifest for some time. Certainly, since there is no tumour as yet, where could the metastases come from? This means that the operation was performed late, in the fourth, usually incurable, stage of the disease. If, however, the tumour had existed for 15 years before it began to grow, then there had been sufficient time to remove it safely, and it can be stated with full assurance that there would not have been any need to count the days remaining.

Non-malignant tumours may also grow but they merely increase in size without penetrating surrounding tissues and they never metastasize. This is why the fact that a tumour has grown for three years is not yet proof that it is malignant.

It is hard to understand why the patient expected to live for only five years. If there was no malignancy, such arithmetic was senseless. If he had a malignant melanoma, then avoiding treatment he lost all chances for a long life. An artificial system of calculation as to what fate has in store is groundless and in no way suitable for making such a vital decision about whether or not to consent to an operation or to refuse, to sacrifice oneself to “crocodiles and cannibals” or to sail off to the sea of quackery and fortune-telling.

Last but not least, let us discuss statistics. People like to cite the same kind of examples as the characters in Soloukhin's story did: one friend was operated on and soon afterwards he died, while another refused and still lives. But in our time how can people juggle with life and death on the basis of rumours and chance, and moreover, of unproven facts!

Solid statistics reveal that correctly treated patients, with melanomas that had no obvious metastases at the time of operation, in 40-53 per cent of cases live five years and longer; in other words they may be considered practically recovered.

In his splendid *Letters from the Russian Museum* Soloukhin expressed the sensible idea that art should be viewed as a pastime.

To some degree medicine is also art, and the application of laws of formal thinking here is not suitable. Without sound preparation in the subject it is both harmful and dangerous to discuss diseases in the press. It is good to be a dilettante (if this can be so expressed) only when contracting a disease.

To be fair, it should be mentioned that even some educated physicians, not only men of letters, use information provided by the mass media to spread hearsay about cancer adding to its legend.

"Why is it that no effective agents have yet been found to prevent such a deadly disease as cancer?" asks a physician and author of popular science literature in a recently published booklet. He answers, "Primarily because the causes of its origin are still not absolutely clear."

Without debating his views regarding the helplessness of oncologists, let us see how he proves his point: "The largest number of cancer patients is registered in New York, the least in Sri Lanka."

Remarkable! A discovery with each sentence! In the first place it is not clear whether he is comparing the two territories with each other, or with other parts of the world. In the second place, we have no inkling of what he is analyzing: the absolute incidence (the numbers of people who fell ill) or the relative incidence estimated per 100 000 of the population. Considering the difference in the population of inhabitants we can only compare the relative figures.

Nonetheless, let us see what conclusions the author draws, referring to "some specialists", in explaining the phenomenon thus brought to the reader's notice. "In New York," he says, "there is too much benzpyrene in the air, whereas the people in Sri Lanka eat very little meat." What a comparison to make!

Since cancer strikes mainly elderly people, it would have been far more logical to compare the age composition of the populations and show that in New York the percentage of people over the age of sixty is three times more than in Sri Lanka, that the average longevity of Americans is about 9 years more than in Sri Lanka, and that child mortality is still very high in the developing republic along with deaths from infectious and parasitic diseases.

But, the book further explains that the crux of the matter is actually neither in meat nor in polluted air; rather "most scientists have now reached the conclusion that cancer is a viral disease". And that's that! In other words people eat less meat in Sri Lanka, but the virus is not found there. It is for this reason that the incidence of cancer on the island is not very high. Another word and one might think that cancer is infectious.

The author concludes his theoretical discourse with the maxim: "While medical experts argue and seek causes, over six million people die annually from cancer." Thus, the blame is laid on the medical specialists who got lost in a sparse forest, while cancer patients have been abandoned to the whims of fate.

The unprepared reader is overwhelmed by a torrent of various, often unproven and sensational reports. There are even reports of successes due to cancer treatments that are still in the stage of research.

"A drug derived from medicinal herbs, developed in three years of research on animals at the Osaka University and the Japan Institute of Oriental Medicine is an effective anti-cancer agent. It consists of 30 different components derived from herbs including grassy peony; these herbs have been borrowed from ancient Chinese medicine and produce a comparatively small number of detrimental side effects.

"Favourable results have been obtained with this medicine in treating carcinoma of the mammary gland, stomach, rectum and uterus.

"This new agent does not destroy healthy cells and most probably has a favourable effect on the general physical condition of patients."

This might have been met with acclaim if not for the postscript to the report published by the France Press Agency on October 24, 1976: "In view of the fact, however, that the anti-cancer properties of the drug have not been fully studied, several years may pass before it becomes widely applied in medical practice."

Why then didn't the reputable French Agency wait out the needed time before advertising the remedy in question? Such misleading articles raise false hopes; somebody might already eagerly be seeking the grassy peony and the 29 other herbs. The years which have elapsed have shown that the victims of cancer have been deeply disappointed.

Such legends can be remarkably enduring. One of them lives to this day thanks to the letter Anton Chekhov sent to the publisher A.S. Suvorin mailed from Melikhovo on January 11, 1897: "... A medicine preventing cancer has been discovered: for nearly a year now the Russian physician Denisenko has been prescribing the juice of celandine (*Chelidonium*) and reports say the results are amazing..." As a cautious physician Chekhov never recommended a new but untested method, and in this case he had merely made a note of it.

Without going into detail, it should be mentioned that soon afterwards, Dr. Denisenko's "panacea" was refuted at a special session of the Society of Russian Physicians in St. Petersburg, where many well-known clinicians described the results of their observations. During the ensuing discussion the famous Russian surgeon N.V. Sklifosovsky emphasized that the application of celandine was just treading on already trodden paths. He noted that in medicine something that had been discovered ages ago and forgotten is frequently rediscovered.

The perceptive scholar proved to be right: later the same herb appeared on the pages of various publications from time to time. Moreover, 80 years later, a similar debate arose concerning the use of celandine in treating rectal polyposis. Once, at a regular session of the Association of Moscow and Moscow Region Oncologists, V.D. Fedorov, Director of the Proctology Institute, who chaired the meeting, was obliged to make the following conclusion:

"We often have to operate patients after they have undergone ineffective therapy with celandine. It must be recognized that this method is theoretically groundless..."

Another example of premature advertising is coincidentally linked with the theoretical substantiation of a method. The case in point is the treatment of cancer with anti-somatotropic serum.

A.F. Lazarev, a biochemist, established that the development of experimental tumours in the blood of animals is accompanied by an increased concentration of one of the pituitary hormones, namely, somatotropin (which promotes growth). Somewhat earlier B.M. Gazetov documented a similar phenomenon in people suffering from cancer. Lazarev believed the solution to be as simple as could be: to retard tumour growth, or to achieve regression, he proposed developing a drug that could suppress the production of growth hormone by the pituitary body.

Significant effort was spent in producing an anti-somatotropic serum, but unfortunately, it did not affect the fate of cancer patients. Moreover, as it later became clear, the tumours themselves proved capable of synthesizing growth hormone. It is quite possible that its surplus in the blood is not the cause but a consequence of tumour development.

This serious scientific investigation was given unqualified coverage in the press—in newspapers and magazines. As a result people were misled and began to obtain this antisomatotropic serum at any price, missing the time for proper treatment.

A foreign weekly came out with an arresting headline: "Has Professor Buzhinsky conquered cancer?" True, the question mark dulled the sensational impact to some degree and gave rise to doubts, but hope could still linger...

This article is typical of publications that address the man in the street.

The author begins by introducing his hero: 35-year-old Stanislav Raymond Buzhinsky who works in Houston. Although the Professor is still very young, the walls of his office are hung with diplomas, medals, and certificates. This "visiting card" is aimed at winning the visitor's confidence in what the doctor has to say. The author of the article himself admits entering Buzhinsky's laboratory "electrified" by the reports in the Washington radio and press regarding the remarkable successes scored by the Professor in the battle against malignant tumours.

The only tangible information that can be derived from all this publicity is that Buzhinsky is engaged in the experimental therapy of malignant diseases. To be more precise, he was able to isolate chemical proteinaceous substances from normal urine, which he named anti-neoplastons and which allegedly possessed an anti-tumoral effect.

In experiments he demonstrated that anti-neoplastons prevent the pathological proliferation of cells; their deficiency in the organism may lead to cancer.

Buzhinsky's research, which has been described in many articles in chemical and medical journals, may eventually find a place in the study of tumoral growth mechanisms, but it is still a far cry from a "victory over cancer" (even with a question mark). And the hazard that somebody might begin treating or preventing cancer with urine remains very real.

For several years now the press in the United States and in some other Western countries has been discussing the possible application of the drug "laetril" produced from apricot kernels. Every year 25 tons of this drug, which has not been approved by the American Medical Association, is used in the United States, illegally imported from abroad. Advocates of the drug claim that it improves the general condition of cancer patients and sometimes even causes regression of the disease. These advocates call for lifting the ban on the drug. Opponents of "laetril" consider its benefits questionable, while the possibility of it causing harm remains without a doubt because physicians have documented cases of poisoning by "laetril", which contains cyanide compounds. The main disadvantage is that patients are led astray and refuse tested methods of treatment.

To grant the reader a respite from such sad medical tales, we offer the following instructive story.

One of the authors of this book, as a young physician and beginning journalist, wrote an article for a popular women's magazine under the sensational title, "Giving Birth Can be Painless". Expectant mothers got excited—they all wanted to test the new painless birth. For several months the phones at the hospital kept ringing, nearly destroying the reputation of the young surgeon in the eyes of his colleagues.

"There's another pregnant woman looking for you," they would inform their young colleague at the most inopportune moments. This experience, if it didn't destroy all desire to popularize medical knowledge, at any rate forced the young doctor to be careful not to advertise unproven methods and drugs.

Whether on purpose or not, the mass media shapes the views of society and, in this way, either promotes the successes of public health care or jeopardises the life of people that fall ill.

A shocking example of the latter case was the "Philippine boom" when thousands of sick people in Europe and the United States were fooled by cheap publicity and rushed to the Philippines in quest of the advertised miracle. Among them were many cancer patients.

The press asserted that as a result of special training the bare hands of a doctor can separate living tissue without harming large blood vessels; such dexterous hands can probe deep in the organism, in the abdominal cavity, for example, to remove a tumour from a diseased organ, leaving no trace on the body, not even the smallest scar.

Professor L. Watson, a British biologist, describes such operations in the most exultant tones, not stopping to think that the manipulations of these "healers" are more like the tricks performed by magicians: "To the amazement of many witnesses they perform miracles of psychosurgery; they do not use either instruments or anaesthesia. Their only instruments are their hands. They know nothing about aseptics and nevertheless there have never been cases of infection or post-operative shock...".

This quote reveals that one does not have to be absolutely ignorant or uneducated to believe in miracles; one can even be a biologist with the rank of professor.

Before commenting on Watson's statement let us note briefly that hands of a surgeon really are his main instruments; while the scalpel, clamp and suturing devices are merely weapons in these hands. As a rule, the surgeon's hands in no way outwardly differ from others except that they are well cared for: there are no bruises or scratches, the nails are trimmed and the skin is clean. In line with their profession, surgeons have delicate hands with sensitive strong fingers. Sometimes such hands are not only dexterous, but also quite expressive. The hands of S.S. Yudin, the outstanding Soviet surgeon, come to mind just as they are depicted by the painter M.V. Nesterov; this remarkably flexible fingers arrest and hold one's attention.

K.S. Simonyan, one of Yudin's pupils, relates how the professor described an operation he had just performed:

"...I cut open the abdominal cavity, put my hand on the tumour, felt all around it and realised that it could be removed... Look!"

His right hand was raised in the air in an impatient gesture.

"I put my hand on the tumour (he opened the palm of his hand), palpated the spleen (his little finger drew a circle in the air) and saw that the peduncle of the spleen was free. I palpated the liver (the movement of the little finger was echoed by the thumb), there were no metastases; I checked the oesophagus (his index and middle fingers made as if encircling the oesophagus) and it was free. Then I checked the posterior wall of the stomach (his hand dropped as it would have onto the keys of a piano). It was mobile, which meant that the tumour was operable..."

Yudin spent barely more than a minute to inspect the organs of the abdominal cavity and decide whether it was possible to remove the tumour completely. He operated very quickly, but nonetheless, he was no match for the Philippine miracle-workers.

Perhaps some reader has seen an amateur film about operations performed without a scalpel or anaesthesia. (We use the word amateur to underline that no scientific film studio is responsible for these films.) The following description is for those who have never seen such a film.

The so-called surgeon, without even removing his watch or rolling up his shirtsleeves, digs his fingers into the abdomen of the patient who is stretched out on an oilcloth covering a plain table. Some liquid, which the commentator calls blood, appears between the fingers of the quack. Nervous spectators are advised to keep their eyes shut. The wound, of course, cannot be seen, but the audience is told that the surgeon is "rummaging" inside the stomach. Minutes later a small piece of tissue appears in his hands (the removed tumour!) which is immediately thrown out. The patient gets up as if nothing had happened, convinced that he has been cured of cancer. The patient next in line takes his place.

After the showing of this film, accompanied by a similar amateur motion picture of parapsychology, one of the authors of this book asked his neighbour, who turned out to be an experimental physicist from a large academic institute, what his impression was of the screening.

"As for the dishes moving over the table under the influence of psychic energy, the switching on of electric bulbs by intensive stares, and other tricks—that was obvious movie magic—but the operations ring true without a doubt."

"But you were shown neither the operation wound, nor the internal organs," exclaimed the doctor in surprise.

"I saw the hands of the quack reaching into the patient's bowels and removing the tumour."

It proved impossible to dissuade the physicist. All I could do was revenge fully:

"As a surgeon I am sure of the authenticity of telekinesis and the transformation of psychic into electric energy at a distance, but I categorically state that the operation was a complete fraud!"

My joke hit the mark.

"To be sure, let specialists judge," laughingly agreed the physicist.

The following is evidence provided by the French journalist A. Ledau, who had been to the Philippines and brought back bits of tissue allegedly taken from the patients by the quacks:

"Histological analysis and microscopic examination make it possible to affirm that these organs and tissues are not part of a human body and are not pieces of cancerous tissue..."

In another case a close inspection of ovaries, which had been allegedly removed from oncological patients "painlessly", established that they actually belonged to goats, and were covered with animal blood.

The French television cameraman Jean Luk Manieron, who had witnessed more than a hundred such operations, focussed his photographic equipment on the hands of the "miracle doctors" and under the operating tables, and succeeded in exposing the quackery. It is no wonder that, since then, the Philippine "miracle healers" avoid demonstrating their "skill" in the presence of medical specialists, journalists and professional magicians.

It should be mentioned that professional entertainers and magicians have many times helped medical specialists to expose charlatans. In a recently published biography about the American Professor Joseph Bank Rayne, considered to be the "father" of parapsychology, which was written by the French journalist Michele Ruse, there is a curious episode relating to the "scientific" basis of telepathy.

In 1927 Rayne was stunned by the talent displayed by a young horse called "Lady Wonder" which guessed unseen numbers written on a sheet of paper. According to his biographer, Rayne was a gullible person and readily cited facts which served to prove his hypothesis about the existence of parapsychological phenomena. Such scholars fit the poet Pushkin's description: "Oh! It's so easy to deceive me! I seem to enjoy being fooled!"

This was the case with the unusual horse whose abilities were advertised by Rayne in his article titled: "Lady Wonder is a Horse that Reads Thoughts". In his description of the experiment, the professor noted that results were not obtained if he wrote the number while standing behind the owner of the horse. The magician M. Christopher made note of this fact and decided to observe the whole procedure not revealing his profession. Christopher pretended to write the number 8, but actually wrote the number 3. The horse pointed to 8. It became clear to the magician that the horse trainer could read the "unseen" figure by the movements of the pencil and that the horse later chose the cube with the right number according to the owner's signals which the audience failed to notice.

Quackery has a long history and tested methods for fooling people. In *Praise of Folly* written 500 years ago, Erasmus of Rotterdam emphasized that the physicians who are ignorant, impudent and reckless are valued most. Moreover, medicine itself, as it is currently practised, is nothing but the art of fooling people.

But how is it possible that an educated person living in the last quarter of the 20th century is capable of being taken in by such supernatural gibberish? It's embarrassing to admit, but people still turn to all sorts of healers and quacks.

"What do you expect, if you, oncologists, can do nothing to help?", argues the sceptic, ignoring the fact that oncology has already achieved a lot. What he wants is the miracle panacea that will deliver humanity from cancer for all time, just as was achieved with the plague, smallpox and other diseases which in their time caused millions of deaths.

One can understand incurable patients who grab for a straw like a drowning man. Such a patient, unfortunately, cannot, like the hero of N.M. Amosov's popular-science novel *Memoirs from the Future*, subject himself to long-term anabiosis (a state similar to winter hibernation of animals) so as to postpone the treatment of his mortal disease until a remedy is found. The advertising, however, is done by healthy not by sick people. What is this? Mass-scale hypnosis?! Or is it our age which has accustomed us to miracles that is to blame? Certainly, ever since a transplant of the human heart was accomplished, one has to be very careful in making unconditional denials in medicine.

Now let us reply to Professor Watson about operating "without a scalpel". It would be strange if these hoaxes caused inflammation of the abdominal cavity or shock in patients. But there can be no doubt that the developing malignant tumour, which they seem to have been saved from, will continue to develop; the curable stage will be missed and the tumour will become incurable. Incidentally in the foreign press sad announcements such as the following are appearing more and more often: A four-year-old child recently died of cancer in the Belgian town of Rocheforte. It was known that his parents did not believe in medical treatment and had appealed for help to Tony Agpaoa, the famous Manila "healer", who promised to cure the infant. For several months the boy was "a living miracle" and flights to the Philippines were full of patients who wished to be treated by Agpaoa, reported the French magazine *Spectacle du Monde* in Paris.

As for the term "psychosurgery" used by Watson, the authors confess that they have never heard of it. Even in fairy tales the surgeon uses a scalpel. Surgical intervention implies the physical invasion of tissues and organs by means of a cutting instrument, high temperature (electrosurgery), freezing (cryosurgery) or a laser beam. It is hard to understand, however, how psychic energy can destroy or separate tissues. This lack of understanding includes the British professor who, according to his own words, is tired of living in a rational world and therefore seeks ways to connect what is natural with the supernatural.

Contemporary advocates of non-scientific methods of medical treatment should be reminded that already, more than 100 years ago, A.I. Herzen called homeopathy a slim truth in an enormous lie and noted with irony that ladies believed in homeopathy only because it was absolutely improbable.

One of the invariable peculiarities of man, states Watson, is his propensity for belief in the mysterious, in a miracle...

In reply to this, the following statement by I.I. Mechnikov, the great Russian scholar of natural sciences, which concludes his book *The Nature of Man*, is sufficient: "...If it is true, as some people often contend, that it is impossible to live without faith, this solemn belief can be none other than faith that knowledge is all-powerful". We are realists, and the daylight of thinking, according to A.I. Herzen, is closer to us than the moonlight of fantasy. Unfortunately, truth grounded on real facts and solid proof is always attended by the shadow of pseudoscience.

During his time, the American psychologist S. Camp published an article exposing the nature of quackery where he wrote that, with every new day, science becomes more complex and specialised, thus making difficult for the non-specialist to comprehend. As a result, the man in the street finds it harder and harder to keep up with scientific discoveries. On the other hand, pseudoscientific myths help the average people who believe in them feel that they are in the midst of the contemporary scientific stream, or that they know something that the next man knows nothing about, without bringing themselves to make any efforts.

Supernatural phenomena have become accepted as commonplace in the West. According to the data collected by Professor David Meyers, almost 60 per cent of all Americans do not doubt the existence of extrasensory perception "on the basis of personal experience".

This same scientist cited a simple but illustrative example. The personnel of the University of California asked a circus magician to show their students a few tricks imitating extrasensory powers. The students were told that the "mind reading" and other parapsychological demonstrations were only majic arts. Nevertheless, most of the audience after the session were sure that the performer had been an authentic "medium".

Myths and legends are particularly strong and persuasive when science blends with the everyday life and experiences of people. In these cases, reference is usually made to well-known historical parallels when outstanding successes were achieved by people who had not received special training.

It is a fact that no so-called "expert" ever attempted to make an important discovery in astronomy, physics or other natural sciences, but many people feel that they know better how to treat cancer or infarct, how to bring up children, write books or stage plays. In the story *le Fils du Titien* A. Musset notes very justly that everything that is truly beautiful calls for long effort and concentration. There can never be true genius without patient labour.

A.I. Herzen compared dilettantes in science with love that begets no children. Moreover, dilettantes hinder others from enjoying true love, distracting scientists to evaluate all sorts of "inventions" and "finds".

It is true that the history of medicine knows many examples when outstanding discoveries were made by people who were not physicians. Pasteur studied the fermentation of grapejuice and discovered microbes, giving birth to a whole branch of science—microbiology. At the turn of the century the physicist Wilhelm Röntgen discovered peculiar penetrating rays capable of making shadow pictures of different objects placed between the emitting tube and a photoplate. Among the first X-ray pictures was that of a human hand. It became possible to look at the organism "from inside" and a new medical science was thus created called roentgenology, the importance of which need not be described. The Curies discovered that radium emits rays and told physicians how to make use of this property. The monk Gregor Mendel studied peas in his tiny monastery garden, and, after precise experiments and calculations, laid the foundations for the new science of genetics which has had a tremendous effect on contemporary medicine.

In these and many other instances, medical science made use of only the by-products of great discoveries in natural science. Neither Röntgen nor the Curies delved into the diagnostics or treatment of patients, and the further development of their ideas in the medical sphere was accomplished by physicians. As for Pasteur, this man of genius attracted great minds to help him such as Mechnikov, Koch, Havkin, and Bezredka, each of whom himself became the founder of a new direction in medical science.

Pasteur's theory on preventive vaccinations was largely supported by the practice of the British physician E. Jenner who prevented smallpox infection by inoculating extracts from cowpox papules. At Pasteur's proposal, the term vaccination acquired a broad meaning and became a synonym for any prophylactic inoculation in honour of the contribution made by Jenner for all of humankind.

Great discoveries occur rarely and only then when there are objective conditions, a sufficient accumulation of facts necessary for making general conclusions, and when there is a scientist capable of synthesizing them to make a new qualitative leap in the development of science. The great Soviet physiologist Academician V.V. Parin stated the following in this respect:

"There are people naive enough to regard a discovery as the result of pure chance which became the subject of meditation and the sudden dawning of a great idea. It has long been known, however, that chance only helps the scientist who is capable of understanding and evaluating such an opportunity. How many microbiologists witnessed the inhibition of the growth of cultures of microorganisms when fungi happened to come in contact with them, but evaluated this fact only from the traditional point of view and threw away the cultures because they were "dirty". Fleming, however, was able to perceive the new phenomenon in principle, namely, the suppression of some microorganisms by the products of the vital activity of others. Along with Florey and Chain he succeeded in separating out the pure active substance, penicillin, and thus inaugurated a new era in medicine, the age of antibiotics."

But let us return to the subject of extrasensory perception.

In order to end the discussion about the "methods of treatment" practised by the notorious Juna Davitashvili, the Science Department of the *Literaturnaya Gazetta* gave a clear-cut definition of the most reasonable approach to such "healers" from the scientific as well as the sociological and psychological point of view:

"In the past twenty to thirty years we have heard of at least several dozen "healers" of diseases who at various times won popular acclaim promising great discoveries. The question is, where are they now? Where are their "methods" and "discoveries"? Has any single one of them stood up to the test of time, the strictest test there is? Alas, all of them, even the most startling, have vanished from medicine's horizon, along with their "methods" and "discoveries"... Medicine is a modern scientific field, but it is not all-powerful. It cannot cure some diseases and it overcomes others with much difficulty. But patients want to be cured at any price. This is their natural desire. Thus, the situation may exist in medicine (and will probably always exist) when "demand" exceeds "supply". In such conditions, as is known, there is a great opportunity for profiteering and for all sorts of sensational "hullabaloo".

Oncology is precisely one of those branches of medicine that easily lends itself to gossip about its successes and failures. Its diagnostic and treatment methods are constantly being improved and cannot possibly be compared today with their levels of 20-25 years ago. It is essential that all the current successes in oncology are based exclusively on advances in scientific knowledge about cancer and in no way on guesses and unproven hypotheses. On the other hand, no matter how strong our desire, we still lack sufficient information in order to develop a general theory. We know a lot about different branches of the science and have penetrated deeply into the biology of the cancer cell and the reaction of the organism, but the stage of synthesis has obviously not yet been reached. The medical treatment possibilities are still insufficient for dealing with cancer patients in the late stages or with certain rare forms of cancer. These objective circumstances are to some degree conducive to the appearance and spread of unscientific methods of cancer treatment.

Among the quacks who get rich on other people's misfortunes and, as a rule, conduct their activities illegally, there happen to be individuals who do not selfishly seek profit and who have a sincere wish to save mankind from this terrible disease.

From time to time our oncological institutes receive letters from people who propose testing various home-grown remedies for treating malignant tumours. Occasionally these remedies are said to be products of folk medicine. Needless to say, from time immemorial the naive belief has persisted among simple folk that an antidote for any poison can be found in nature.

"Fire can be countered with water, a mouse can be dealt with by a cat and a remedy can be found for any disease," explained an elderly collector of herbs in Bryansk about how to battle cancer. More often than not, these remedies are so primitive and crude that no test is even necessary to prove their uselessness. As a rule, the authors of such letters never insist on subjecting them to tests. When there is an inkling of rationale in any such recommendation, experiments are performed on animals.

Any innovation in medicine must be scrupulously tested and investigated before it is applied to clinical practice.

The testing of a new medicinal agent on a patient is an extraordinarily responsible act. According to Soviet laws, each case is strictly controlled by a special order of the Ministry of Health and may be permitted only after close and detailed study. The test is carried out in several stages, consecutively determining the maximum permissible dose of the given agent, its antitumoral activity, the range of effects and a rational schedule of application.

At the first stage, patients are selected whom the experiment cannot harm under any circumstances. All the details are carefully worked out beforehand. Since it is not known whether or not the given agent produces side effects, the initial doses are very small. To avoid the risk of simultaneous complications in several patients, each of them is placed under observation after certain intervals. The dosage is increased gradually and only after the physician is assured that the initial or previous dose caused no harm.

If the preparation shows promise during primary tests, it is given to new groups of patients in less advanced stages of cancer. If there are no favourable results the patients are immediately referred to chemotherapy which has proved to be effective.

Nevertheless, it still occurs that much excitement is stirred up around dubious findings and the authors of these questionable methods, sometimes backed by the press, attempt to bypass lawful restriction. Nothing can be more hazardous for innocent people than impudent ignorance!

These authors had the opportunity to learn in detail about the results of an investigation of the widely advertised cancer cure proposed by Guman, Prodan and Kachugin, which caused quite a stir 10-15 years ago, but is hardly remembered today. The advocates of the method claimed that they had discovered radical ways for the treatment of malignant tumours. Controlled tests of their "methods" carried out in a clinic, following strict rules for establishing the diagnosis and controlling the effectivity of the drugs, revealed nothing but a sham.

The inventors of these methods put up a fight. They tried to explain away that the poor results were due to the fact that during tests they were allowed to treat only patients in advanced stages of illness.

Earlier, however, they had claimed that they could save cancer victims who were on the threshold of death. If such a claim is made, it is natural that the treatment be tested on the corresponding group of patients. In addition, modern oncology already possesses reliable and effective remedies for less advanced stages of cancer.

Physicians in the past used to say that one must never prescribe treatment that the doctor himself would not agree to undergo. But the authors of this book remember an incident many years ago when a famous "healer" brought his wife, who was suffering from a malignant tumour, to the clinic of the Moscow First Medical Institute and requested that she be treated by the generally accepted method. Incidentally, this led to the complete exposure of the quack.

Recently the Ministry of Public Health of the Russian Federal Republic assigned one of the authors of this book to "investigate" the activities of S.E. Chernyshov, an inhabitant of Sochi. Chernyshov was an elderly retiree, a builder by former profession, who for approximately 25 years had a private practice in his home treating any disease without exception with an "elixir" that he had concocted himself and which he claimed consisted of products of his apiary.

Local authorities attempted to bring Chernyshov to trial charging him according to Article 221 of the RSFSR Penal Code for illegal medical practice, but the court came to another decision. It was noted that since "Chernyshov is of elderly age and that his infringement of the law was insignificant and without severe consequences, but, on the contrary, the pills and drops he supplied had a favourable effect on patients, administrative rather than criminal actions would suffice."

This light sentence was undoubtedly influenced by the intervention of a popular magazine. In December 1979, when Chernyshov's case was under inquest, the magazine's editorial board met with him to discuss the subject. According to the court investigation, Chernyshov was far from unselfish in his efforts, gaining national publicity through the magazine and, thus, increasing the deluge of patients searching for the "wonder elixir".

Chernyshov tried to substantiate his method "on theoretical grounds", publishing articles and whole theses on the subject. In his articles he slandered medical science in all possible ways, contrasting it to folk medicine, which he termed "demopathy" in order to disguise the obvious fraud. (Incidentally the term "folk medicine" is often used as a cover-up for pure quackery. This is why the authors insist that Chernyshov and his ilk be called quacks.) The following is an example of Chernyshov's reasoning:

"...In amputating or irradiating this or that part of the human body, mechanopaths (as he calls doctors.—*Authors.*) actually create invalids, and we do not censure them for this but actually admire their skill. What skill? The skill to create invalids? Whereas the demopaths who cure such patients without causing them any damage are brought to court as criminals!"

"Demopaths" like Chernyshov publicize "simple, universal and painless" methods of treatment.

"Chernyshov's elixir is a medicine curing any disease, it is an agent that eliminates waste products from the body regardless of their properties and the place of their residue therein, whether in the cells of muscles, tissues or the cells of the haemopoietic or circulatory system. It simply removes residual waste from the organism, making it pure, and therefore, healthy. What is most important is that there are no contraindications for the elixir, which signifies an absolutely new approach to the human body, a new trend in therapy, a new landmark in the history of medicine that reveals how we can be rid of diseases by flushing them out rather than killing them. This is a method of treatment that does not cripple. This method demonstrates directly and unambiguously that it is time to turn the page in the history of medicine and start anew with a clean page and another chapter."

To be sure, everything is very simple.

Academician A.B. Migdal clearly defined the persistent indispensable characteristics of pseudoscience: an intolerance of refuting arguments, ignorance and anti-professionalism obvious to any serious specialist, and aggressiveness. One can see that Chernyshov's statements, just as those by Kachugin, Prodan and others that we cited, easily fit the description given by Migdal. He took a fierce stand against pseudoscience in quite another field, but it seemed as if he had read the letters of these would-be oncologists and their advocates among the press. Migdal's arguments are so much to the point, that one cannot resist quoting them.

"Pseudoscience tries to prove it is right fighting with no holds barred. It is possible and necessary to protest against unjust evaluations of research, but only scientifically accepted methods should be used to influence public opinion.

"We cannot seriously accept allegations that pseudoscience is being unjustly dealt with. At all times in history pseudoscience has hounded science and to assert the contrary would be tantamount to a lack of respect for the memory of all victims of pseudoscience, starting with Galilei.

"Naturally, articles that refute the scientific method of cognition are also irresponsible, aggressive and pretentious."

Chernyshov's proposals were examined by the AMS of the USSR, the Board for the Introduction of New Medicinal Agents and Medical Technology of the USSR Ministry of Health, and the Pharmacological Committee. All these authorities were unanimous in their negative evaluation of Chernyshov's invention and he was warned that it is impermissible to deceive patients as he was doing.

The firm and uncompromising stand adopted by these high offices by no means indicates that the experience acquired by folk medicine can be ignored. Many medicinal plants (Lily of the Valley, foxglove (Digitalis), Valerian, Cudweed and others) which are currently widely used in therapy were taken from folk medicine after being cleared of any remains of quackery. The exaggerated role of folk medicine before the Great October Socialist Revolution stemmed not from its ability to "work wonders", but primarily due to the great lack of physicians and the high cost of drugs. The following explanation was given by M. Nosal, who devoted 45 years of his life to the collection and study of medicinal herbs: "When a village is located 30-40 kilometres from a town where there is a doctor, and the nearest doctor's assistant lives at least 15-20 kilometres away, it is no wonder that a sick person, surrounded by the autumn or springtime country mire through which few roads pass, resorts to medicinal plants as remedies, and appeals to me, because I live nearly and know about these plants."

The USSR Institute of Medicinal and Aromatic Plants has been founded in the USSR which functions very efficiently. The "gifts of nature" must be separated not only from the remains of quackery but also from all sorts of alien and harmful admixtures. Active substances produced from plants, which are characterized both chemically and physiologically, are required in medical practice. Let us recall the history of malaria treatment. For many years patients were given giant doses of cinchona tree bark suspension, until in 1816, the Russian chemist F.I. Gize isolated quinine as its active component. This discovery considerably simplified the treatment of malaria and promoted the synthesis of more valuable anti-malaria preparations.

In recent years more interest has been focussed on the Oriental pharmacopoeia with its rich abundance of exotic prescriptions borrowed from ancient treatises. Research at the current level of experience that has accumulated over the millennia can expand the arsenal of contemporary medicinal agents. I.I. Brekhman, D.Sc. (Med.) at the Marine Biology Institute under the Far Eastern Scientific Centre of USSR Academy of Sciences processed by computer prescriptions based on a vast amount of plants and an even greater number of combinations. Analysis of this data resulted in the selection of the so-called "healing nuclei", i.e., limited groups of plants producing a pharmacological effect in certain diseases, which were subject to more intensive research.

It often happens, however, that the recommendations of folk medicine, particularly concerning serious diseases, are harmful simply because they distract the patient from the required treatment.

It is appropriate here to quote Paul Lesh, a prestigious French specialist and President of the International Congress of Pharmacologists, who was interviewed several years ago by V. Mikhailov, the scientific observer for the *Literaturnaya Gazetta*: "...folk remedies may be used until they begin to interfere with the active treatment of a patient. If, in the case of cancer, the patient hopes to improve his condition by means of tinctures and thereby refusing effective, although dangerous, agents, he is committing a crime against his own health. The same should be realized by people suffering from any severe disease. No one should harbour such illusions, because in these cases, "healing by herbs" may end in death..."

The case histories of some inhabitants of Sochi are sad proof of this. They spurned the "services" of the local oncological clinic in favour of Chernyshov's much advertised method and all died rather quickly. In the Haematological Department of the Clinic, the authors observed a young man suffering from lymphogranulomatosis, a malignant disease of the lymphatic system, which is already being successfully treated by drug and radiation therapy. The diagnosis had been made at the Leningrad Roentgenoradiological Institute where a course of effective chemotherapy administering half the dosage of radiation therapy had already been started. Everything would have been fine if the parents of the youth had not been swayed by articles in a popular magazine which induced them to take their son to Sochi where he was given Chernyshov's "magic elixir" for four months. He was finally hospitalized at the local oncological clinic in very severe condition with an obviously progressive disease.

During a personal discussion with Chernyshov himself, in the presence of two very prestigious Sochi physicians, the healer admitted that not all oncological patients survive treatment by his method. When he was asked to name at least one person he had cured of cancer, he provided several names. It turned out that none of the inhabitants of Sochi that he named had ever been examined by specialists, nor had the diagnosis of a malignant tumour been reliably established.

When the authors were completing this book, the newspaper *Sovetskaya Rossiya* informed that Chernyshov had been found guilty of fraud and had been arrested. It is now known for certain that his "elixir" was composed of alcohol, water, unslaked lime and salt, coloured with green tea or Cardiaca vulgaris. According to chemico-pharmacological specialists, "the analyzed liquid cannot be used as a therapeutic agent for the treatment of any disease."

Such self-appointed healers spare no effort to disprove the conclusions of qualified commissions, resorting to pseudoscientific statistical data, whereas serious analysis shows that in the majority of their "patients" the diagnosis had not been confirmed by the morphological method, which provides the only reliable proof of the existence of cancer.

The authors of this book once presented a report at a joint session of the Moscow Surgical and Oncological Societies discussing the types of errors made by physicians in diagnosing and treating oncological patients. A particular type are the so-called errors of hyperdiagnostics, when, at some medical establishments, cancer is diagnosed without sufficient basis. Only subsequent follow-ups and scrupulous examination of patients make it possible for physicians to establish the true nature of the disease and reject the ominous primary diagnosis.

The fact that such errors are sometimes made by even the most experienced specialists, when morphological methods are neglected, is illustrated by the following case:

The mother of a famous Soviet surgeon became ill, and on the basis of X-ray examination, doctors decided that she was suffering from carcinoma of the stomach. The operation was performed in the presence of her son by his brilliant colleagues. They discovered a tumoral lesion of the entire stomach, enlarged and dense lymph nodes in all the basins of metastasis and insemination of the peritoneum. The diagnosis seemed too obvious, therefore biopsy was not performed. Nevertheless, the elderly woman lived for another ten years after the operation. Autopsy revealed practically complete regression of the process, while histology showed that the woman had suffered from tuberculosis of the stomach and peritoneum.

Such errors (let us call them "lucky") occur from time to time. Now imagine that such a patient with unconfirmed cancer appealed to an illegal "healer" for treatment. This would be a real trump card for a quack!

In many cases the improved condition of a patient, or even a short prolongation of life may be explained by psychotherapy and the use of generally invigorating agents following radical treatment. It has now been proved that a sanatorium regimen, completely balanced nutrition, and simple tonics reduce the probability of relapses and metastasis of the tumour. On this basis, special departments for supplementary treatment and medical rehabilitation are being established. Such a ward is successfully functioning at the Scientific Oncological Centre of the USSR Academy of Medical Sciences. The Rostov Oncological Institute has been using a sanatorium at Zheleznovodsk for the same purpose. At one of the Moscow district clinics physicians use psychotherapy and hypnosis to alleviate the suffering of their most severely ill oncological patients.

As has already been emphasized, pseudoscientific methods of treatment may cause irreversible harm simply because the patient is led astray from the proper treatment he actually needs. In a Paris television broadcast, the famous French physician Jean Monier related how he had witnessed the death of women suffering from carcinoma of the mammary gland, although they could have been saved if they had been operated on in good time. On the advice of quacks they had rejected surgery. The physician aptly compared "those who practice free medicine" with inexperienced drivers speeding in a car on Sunday outings.

In 1977 a woman with cancer of the mammary gland entered an oncological clinic in Moscow for help. Although the carcinoma was still at a curable stage, the patient did not consent to an operation and ignored the invitations of her district oncologist. She subsequently moved to another address and thus escaped medical observation. Two years later, her brother, who was greatly alarmed by the state of her health, came to us for consultation. We examined her and were shocked. In place of the mammary gland there was a large gaping ulcer surrounded by multiple daughter nodes of the tumour. The cancer had metastasized to all the groups of lymph nodes. The case was beyond help. It turned out that for two years the patient had been treated by a "herbal healer" who had warned the poor woman beforehand that first the tumour would grow numb, then it would putrefy, open, and the pus would exude naturally. The poor woman saw that the process was developing as her "healer" had predicted and suffered patiently believing the treatment was correct. The most terrible aspect of this sad story is that the quack was perfectly aware of the torture she was inflicting. We managed to discover the address of the quack and report the crime to the authorities.

According to data collected by Martin Gross and published in his book *The Doctors*, more than 100 000 people are victimized by quacks every year. A museum of quackery was actually opened in St. Louis, Missouri with exhibits of devices used for "healing" that eventually proved useless and even harmful.

Soviet people are protected by law from quacks, who have no medical training, and are entitled to highly qualified medical treatment. Even if the patient himself or his relatives wish to gamble with hazardous experiments, medical specialists are bound by law to prevent this. The national system of approbation of medical preparations and the ban on using agents unapproved by the Pharmacological Committee play a vital role. This is an example of the true humanitarian concern in the Soviet public health system.

The best antidote to quackery and pseudomedicine, however, lies in the development of the general culture of the population, the achievements of science and the increasing confidence in physicians. Oncologists are deeply interested in finding ways to conquer "the disease of our age". No one contributes so much effort and labour, even devoting their own life to this goal, as the medical specialists who are responsible to their society for the prevention of cancer.

The Main Condition

There are two main tasks in the struggle against cancer: the decrease of the incidence and the reduction of mortality from the disease. Although the first task depends on overcoming the difficulties in discovering the causes of malignant tumour formation, the second task is already being solved. It is appropriate here to recall the Russian saying: "To save a drowning man, it is not necessary to know who pushed him into the water."

The solution of the second task greatly depends on finding highly efficient methods of treatment and early diagnosis. Moreover, today precise diagnostics come to the fore because the existing methods of treatment have fully demonstrated their value, provided that no time has been lost from the very start.

Four stages are distinguished in the development of cancer, each of which has specific characteristics for the given localization. Typically, however, the first stage is characterized by the presence of a small tumour and the absence of metastases, and the fourth and last stage, the spread of the tumour to the surrounding tissues and extensive metastases. The second and third stages are interim between these two.

Treatment results are clearly dependent on the stage of development of the disease. In the first stage of carcinoma of the lower lip, for example, full recovery is achieved in more than 90 per cent of patients, in the second stage, in 61 per cent, and in the third stage, in only 46 per cent. In carcinoma of the mammary gland the corresponding figures are 90, 55 and 23 per cent. Similar data exist for cancer of the uterus, lung and other organs.

Professor B.E. Peterson analyzed the effectiveness of surgery in carcinoma of the stomach depending on only one component characterizing the stage, namely, to what depth of the stomach wall the tumour had infiltrated. If the tumour is localized in the mucosa alone, resection of the stomach yields 100-per-cent success; if the carcinoma reaches into the submucosal layer, the same operation yields only 93-per-cent recovery. Penetration of the tumour cells to the muscle layer reduces the chances for success to 70 per cent, and if the entire thickness of the stomach is affected, the chances of recovery are reduced to 20 per cent.

Thus, the early diagnosis of cancer is of primary importance in oncology. Unfortunately, as yet, cancer in many patients is discovered when it is in the fourth stage, when it is already too late to apply special methods of treatment; patients with cancer of the third stage are even more frequently discovered, when it is already difficult to hope for stable favourable results.

For several years now Soviet clinics have drafted a “record of neglect” for every case of cancer discovered at a late stage. Based on thousands of these reports it is possible to conclude that there are three principal reasons for the late discovery: a latent development of the process (the most frequent cause), delayed first visit to the doctor, and errors made by physicians.

Let us examine these reasons in reverse order.

If oncologists are to err less frequently, they must, of course, improve their qualifications and skills. There are no basic differences in diagnosing cancer or some other nontumoral disease. The real difference is in the consequences. This is why all erroneous cases are so scrupulously discussed and analyzed at medicial conferences and it is gratifying that the number of such mistakes are becoming consistently fewer each year.

What about the patient himself? People typically do not closely observe their organism. The constant hectic pace of life does not allow one to take care of oneself. The preclinical period of the disease is screened from the eyes of the non-specialist: a developing tumour is still very small and lies hidden. It is only when alarming symptoms appear that a person consults the doctor, but the earliest stages of the disease have already passed. This is why the efforts of physicians and public health care workers are currently directed at detecting the disease in people who consider themselves to be quite healthy.

At first the tumour grows very, very slowly, contrary to the general opinion that it progresses rapidly (this happens later, when the malignant neoplasm is already sizable). It has now been definitely established that the latent preclinical period of growth lasts from 4 to 12 years. In this period of time the tumour may give no sign of its existence.

The question is raised, how can the tumour be detected at precisely this early stage? First of all, it is absolutely necessary to organize regular prophylactic examinations of persons entering their second half of life, and to teach the population to immediately consult a doctor as soon as they do not feel well.

There may be objections to this recommendation, claiming that any person reaching a certain age, for example, 40 years, will then continue to live as if under the sword of Damocles, and this will give rise to mass cancerophobia.

This argument seems justified, therefore, let us examine it in greater detail.

Cancerophobia is classified as a psychological disturbance that may sometimes develop into a severe form, as described by the following story.

Professor V.V. Uspensky worked for many years in Kalinin. He belonged to the legion of Russian surgeons whose professional careers began in an old Russian country hospital. He was an excellent specialist, a bright personality known for his exceptional professional honesty, although he retained his own peculiar way of thinking that is reflected even in his surgical journal: instead of writing in a dry professional tone, the professor used to describe his operations in the literary style of a novelist.

Soon after Professor Uspensky died one of the authors of this book who practised in Kalinin was visited by a female patient who wished to undergo surgery on her stomach because she suspected a relapse of cancer. The woman was very insistent and after some time she was admitted for an examination. Although she assured everybody that Professor Uspensky had operated and removed part of her stomach, X-rays showed, to our great surprise, that her stomach was intact. In the professor's records the following note was found:

"At the insistence of the patient who thought she was suffering from carcinoma of the stomach I opened her peritoneal cavity. As it might have been expected, there was nothing in the stomach of the hysterical woman. The peritoneal wall was sutured tightly."

The patient had read much medical literature which fed her imagination and made her believe that she was really stricken with carcinoma of the stomach. Although Uspensky had a testy character and the patient had tried his patience to the limits, he found a good way out of the situation. At that time X-ray equipment was far from perfect and, when cancer of the internal organs was suspected, the diagnosis could only be confirmed by surgery.

Another case of cancerophobia with a sad end was reported several years ago by N.I. Krakovsky, a Corresponding Member of the AMS USSR, in an article published by the *Meditsynskaya Gasetta.* A well-known professor was visited by a female patient who insisted that she be operated on. Neither previous nor immediate diagnostic examinations revealed any signs of a malignant neoplasm. The professor informed the patient of this and refused to perform an operation. The woman interpreted his refusal as an acknowledgement that she was mortally ill and within a few minutes committed suicide, throwing herself out of the window of the clinic.

Autopsy proved that the professor had been right, but he nonetheless felt responsible for her death because, although the diagnosis had been correct, he had failed to estimate the severity of her psychological condition.

Cancerophobia, as a rule, takes on a lighter form, expressed merely in the fact that the person suffering from this phobia avoids medical examinations, fearing that the doctors will diagnose cancer. It is often the consequence of obtuse, inept advertising of prophylactic measures, which resorts to intimidation in order to achieve its purpose, like the ad for an insurance company which warns, "While you are at the cinema, your house may be on fire. Don't forget to insure your property!"

Associating with people who suffered from cancer and recovered may help overcome cancerophobia. Steps are being taken in this direction. In one of the programmes of the Soviet T.V. series "Health", former oncological patients who had completely recovered from the disease took part. Statistics collected by Moscow polyclinics revealed that after this programme had been shown there was increase in the number by people requesting prophylactic examinations. Such programmes, evidently, should be broadcast more often. In the USA, for example, there is a Club for former cancer patients, the members of which speak regularly over the radio and appear on T.V., providing unquestionable evidence of the successes of modern oncology.

Not long ago a panel of WHO experts acknowledged that attempts to conceal the presence of cancer are harmful, whereas, fears that the medical education of the population might give rise to cancerophobia are totally unfounded.

The testing and detection of patients

with early stages of malignant tumours is promoted primarily among persons in the "precancerous group". This term is not very appropriate because the development of cancer against the background of precancerous conditions does not necessarily take place, but is only a possibility.

There are many precancerous diseases. Among them are polypoid proliferations of the mucosa of different organs, chronic ulcers and erosions, and chronic inflammatory processes in the lungs, stomach, and intestines. The factor they share in common is long-term development and the presence of foci of atypical tissue proliferation where cancer may originate. Several years ago, the staff of the Moscow and Leningrad Oncological-Institutes organized the following "action" in their cities. The white- and blue-collar workers of large enterprises who had been registered in their sanitary departments as suffering from chronic diseases of the stomach were selected for detailed medical examinations. Teams of doctors closely examined them (the teams included a highly skilled oncological surgeon, X-ray specialist and a specialist in endoscopy). This comprehensive examination proved to be extremely effective. Most importantly it detected several patients with the earliest stages of cancer of the stomach which can without a doubt be cured. If two to three years had passed, it would have been too late for treatment. Moreover, there turned out to be a comparatively large number of people with precancerous stomach diseases. Appropriate therapy was prescribed for this patients.

Thorough examinations at dispensary clinics are currently being promoted everywhere.

Let us examine breast cancer. It has been estimated that about a quarter of a million women die from it in the world every year; in the USA this mortality is only comparable with the mortality of women in road accidents. In his very interesting book titled *Facts, Achievements and Failures in Modern Oncology*, Professor A.M. Garin makes public some very impressive statistics: in the United States three new cases of breast cancer are diagnosed and one woman dies from this disease every 17 minutes. It has been predicted that breast cancer will develop in every fifteen-year-old girl who is living in the country today.

It is common knowledge that the mammary gland is one of the organs whose structure and function are affected by the hormones of the hypophysis, ovaries and several other internal secretory glands. Like leaves, which, depending on the season of the year, grow or fall leaving the branches bare, the lobules of the mammary gland, depending on the hormonal equilibrium, either appear or vanish emptying the ducts. This rhythmic development of new lobules is, in principle, very similar at different ages," descriptively wrote the Leningrad morphologist D.I. Golovin.

If the hormonal equilibrium is disturbed, practically all the morphological elements of the gland look as if they are reflected in a distorted mirror. Sometimes nodal formations appear in the tissue, which are capable of regenerating into cancer.

There is a strict rule in oncology: any tumour in the mammary gland must be painstakingly inspected so as to exclude the possibility of cancer. At times one must resort to surgical removal of part of the gland for microscopic study, and this is a "must".

Every woman has a keen awareness of her breasts and can easily determine even the smallest changes in size, shape and consistency. She need only examine herself carefully and regularly. If she does this only occasionally, the disease may be discovered in an already advanced stage.

The expediency of self-examination is obvious, but even more effective is a systematic qualified check-up of the mammary glands by a specially trained midwife at a polyclinic (no less than once a year). X-ray examinations are also helpful. Neither one of these methods rivals the other, just as neither is guaranteed to be perfect, and only their joint application reduces the probability of error.

It is necessary here to briefly discuss pigmentary tumours.

According to poets and artists the mole is an attribute of feminine beauty. Recall Alfred de Musset's story *La Mooche* where the author describes how the hero of the story admired Madam Pompadour's mole. Little did he know, that one of the most malignant tumours—melanoma—may develop (fortunately very rarely) from a mole.

The development of melanoma is most frequently facilitated by a trauma. This should not be forgotten. If the mole happens to be in a place on the body where it is subject to constant injury, it is best to have it removed by an oncological surgeon. By no means should any attempt be made to get rid of the mole by oneself.

It has already been mentioned that far from all malignant tumours arise against a background of chronic diseases; cancer may develop quite independently (in about half of all cases). How can early diagnosis be organized in the cases? How can the doctor find, among the huge number of diseased people, those who are ill but do not suspect this themselves? Widespread examination? This is certainly a laborious task, given the population of the Soviet Union. Moreover, such examinations must be conducted without taking the patients away from their jobs and using methods that do not require spending a large amount of time and special conditions. It is no wonder that the first widespread prophylactic examinations yielded poor results: only a meagre percentage of diseased patients were discovered. Ways to increase the efficacy of this work are being consistently promoted.

The numerous diagnostic tests regularly offered at laboratories (immunological, biochemical, allergy) are not specific and have not proved their value as yet. In many urban communities a questionnaire method is being tested. This is based on the fact that there are certain symptoms which allow people to be grouped based on an increased risk of succumbing to one or another form of cancer. The age, sex, habits that are detrimental to one's health, and early symptoms of the disease which a physician can recognize are taken into consideration. These symptoms are included in the questionnaire which is then distributed among the employees of large enterprises. The forms are filled out and processed by computer. The people singled out based on analysis of their answers are consequently called in for more comprehensive examinations.

A British magazine in the 1970s jokingly published a "prayer" for the middle-aged which contains serious thoughts:

"Dear God! You know me better than I know myself. Keep me from voicing my opinion on any subject at any time. Keep me from the bad habit of telling others what they should do..."

Apart from the appeal to God, there can hardly be any objections to the rest of the prayer; however, oncologists will hardly be able to agree to preventing people from complaining about their pains and ills simply because they may increase with age and the elderly may seem to enjoy talking about them again and again. Paying close attention to changes in how one feels from day to day, the more so for elder people, may aid early diagnosis; therefore, one should not tire reporting to doctors and they should constantly lend an ear to the patient's complaints.

From time to time one is amazed how a person can within the space of a month be utterly oblivious of obvious symptoms of disease. This psychological phenomenon is so common that it has been given a special name —negation of the existence of the disease.

Very often the character of a sick person changes. This was accurately noted by Lev Tolstoi in his story *The Death of Ivan Ilyich*.

"...Everybody was healthy. One could not consider Ivan Ilyich ill simply because he spoke of a strange taste in his mouth and that he had a queasy feeling in the left side of his belly.

"But it so happened that this queasiness began to increase and although it did not develop into pain as yet, he was conscious of a constant heaviness in his abdomen and was therefore always in a bad mood. This bad mood kept intensifying and soon began spoiling the pleasant life reigning in the Golovin family. Husband and wife began quarreling more and more often, the peaceful atmosphere was disrupted, and people were barely polite to one another. Rows occurred more frequently. Just a few quiet islets were left which the couple could share without losing their tempers. Praskovya Fedorovna certainly had grounds now to say that her husband was of sullen temper... He used to start picking at her just before dinner was served and particularly when he began eating his soup. He would either remark that one of the dishes was cracked, that the food was not to his liking, that his son sat with his elbows on the table or that his daughter's hair was not combed. He blamed Praskovya Fedorovna for everything. At first she argued and made unpleasant retorts, but then once or twice during dinner he flew into a rage and she realized that he felt sick from eating and she learned to keep her temper and did not argue, merely telling him to finish his dinner."

Lev Tolstoi does not give only a psychological portrait, but also a most precise description (from the medical point of view) of the first symptoms of carcinoma of the gastrointestinal tract. Approximately fifty years later these symptoms, which had been so accurately noted by such a writer of genius as Tolstoi, were developed by A.I. Savitsky, based on a vast number of clinical observations, into a concept termed "the syndrome of subtle symptoms".

The oncological patient is characterized by a continuing mounting of symptoms. There are some exceptional periods, however, which are marked by a temporary lull: at this time the organism is adapting to the tumour. In carcinoma of oesophagus or cancer of the cardia, disturbances in the passage of food are not keenly felt, in carcinoma of the large intestine, evacuation of the intestine improves periodically. This may lull the vigilance of the attending physician and delay the establishment of the correct diagnosis. Therefore, with the first complaints that arouse suspicion of serious discomfort in the internal organs, the patient must be hastily referred to detailed X-ray and endoscopic examinations.

It is also essential to pay attention to the following, even at the stage of a small tumour. Unexpectedly for both the patient and the attending physician, the picture of the primary chronic disease begins to change: new symptoms appear, which are quite unusual for the patient. Patients should be no less apprehensive when there is an absence of response to treatment that had formerly been helpful.

Among the contemporary methods for detecting cancer an important role belongs to the ordinary but scrupulous medical exam because approximately half of all tumours are visible to the eye and may be palpated and examined. These are tumours of the skin, mammary gland, oral cavity, the lower lip, external sexual organs, cervix of the uterus, rectum, superficially located lymph nodes and the thyroid gland.

At clinics, special rooms for such medical exams have been established and are staffed by trained doctors' assistants and midwives. It may seem strange to the reader that such responsible functions are entrusted to medical personnel with only secondary school training, but experience has shown that cancer and precancerous conditions are revealed in such medical examination rooms far more frequently than in any other subdivisions of the prophylactic network. This is partly due to the fact that the cytological method of investigation is widely used in these facilities and it is simple and dependable. For example, it helps to establish the diagnosis of a developing cervical carcinoma when the tumour is so small that it cannot be seen by the eye.

The cytological method did not win universal recognition all at once. It is still argued whether cytologist are just laboratory specialists studying the cellular composition of blood smears, or pathologists who are interested not so much in the form and structure of individual cells as in the mutual position of cells and their relation to surrounding structures. In making a diagnosis, the cytologist constantly checks his conclusions against the data obtained from microscopic study of tissue sections.

With the practical introduction of the cytological method, scientists now hope to accomplish a complete victory over carcinoma of the uterus; since it can be detected at the very start, it can be cured with a 100-per-cent guarantee by means of a minor surgical operation. The fact that this is possible has been demonstrated in many countries where the cytological method began to be widely applied before being introduced in the USSR. According to the data of the American Cancer Society, in 1945 (prior to the introduction of the method), mortality in the United States from carcinoma of the uterus was 23.5 cases per 100 000 of the population; by 1955, this index was reduced to 11.9. Similar results were produced in Japan, Canada and Norway.

In the USSR due to prophylactic examinations along with application of the cytological test, physicians practically no longer have the unpleasant duty of reporting neglect in the treatment of carcinoma of the uterus. Women should keep in mind that as soon as they are 30 years old they should undergo regular gynaecological examinations. Detected in good time, the disease can be completely cured. Unfortunately, many people are still unaware of this fact and carelessly believe that a tumorous growth cannot happen to them. It is those people who even complain when, according to the new procedure, they are sent for testing and an exam prior to being received by the doctor. This is a typical reaction to a new requirement, which calls for additional, although minimal, time and effort.

This reaction reminds one of the reaction of people to the underground passageways built in Moscow for crossing the street. People thought it tiresome to go down and then up again, when the other side was within easy reach. It has now become obvious to all that such a simple measure is convenient for traffic and ensures the safety of the pedestrians.

In the USSR over 100 million people undergo prophylactic medical examinations every year. The number of cases of disease that are thus actively detected is increasing all the time. In many regions of the country this number has tripled during the last 10-12 years, but in the country as a whole it has not yet exceeded 10 per cent of the number of those who are ill. The efficiency index is no higher than that of an old steam engine. This would truly be sad if not for the thousands of people who have been saved.

Why is the efficiency index of this labour-consuming work still so low? Organizational defects are partly to blame. For example, the same contingent of workers at an establishment are examined year after year. Moreover, most of the employees are young, at an age when cancer is least probable. This phenomenon reminds one of the reverse incidence which occurred once in a provincial theatre of old Russia.

The stage director of the theatre decided to stage a play where there were several scenes calling for many extras. He applied to the colonel of the local garrison to lend him a unit of soldiers for the purpose. The colonel agreed to help, but he sent a fresh unit of soldiers to every new rehearsal... In our case, however, the management involved often directs the same people to be examined, while the rest are never checked by a doctor.

The main reason for such low efficiency, however, is the insufficient set of objective methods used on the medical examination. Although cytological analysis and fluorography are widely applied, their possibilities are limited and scientists are consistently working to increase their efficacy. The example of the application of fluorography for examining the organs of the thoracic cavity explains this problem more clearly.

This method was established for the detection of latent forms of tuberculosis, but when the disease was eradicated as a widespread affliction, the method began to be used more and more often for diagnosing cancer of the lung in its primary stage. Widespread and proper application of fluorography makes it possible to detect up to 30 per cent of the cases of disease. What about the remaining 70 per cent? Why is it that a person may pass the fluorographic test in January, but, in May, doctors discover that he has lung cancer, which, of course, had existed earlier and should have been visible on the fluorogram? Moreover when the old fluorograms of patients are examined once again it is discovered that changes had existed a year or even two years previously, but escaped recognition. Why is this so?

An experiment was conducted to answer this question. Several experienced X-ray specialists, including a famous professor, were requested to inspect a series of fluorograms (the diagnoses were known beforehand, but the participants of the experiment had not been informed of this, of course). During the first hour the answers were all correct. Subsequently, those who were examined became tired and the percentage of errors increased consistently with every hour. Towards the end of the day, even the professor admitted about half of the erroneous conclusions.

Fatigue, of course, is not the sole reason for committing errors. There are also objective difficulties in diagnostics such as the quality of the fluorograms, the qualifications of the X-ray specialists, and, in addition, the maximum of the resolving power of the method itself. Nevertheless, all other conditions being equal, during the first hours of work X-ray specialists made few mistakes, and if they failed to establish a precise diagnosis, they nonetheless correctly separated pathological fluorograms from those that were normal. Generally speaking, this was sufficient, because any changes detected resulted in summoning the patient for a thorough examination.

When this was established, the idea arose of "teaching" a computer to decipher fluorograms. The computer would separate normal from pathological cases and physicians would handle the cases from there.

More than 100 million fluorograms are taken in the USSR every year. Imagine that doctors would have to examine all of them. It would truly be like looking for a needle in a haystack! The efficiency would certainly increase if X-ray specialists would only have to study the fluorograms after they had undergone preliminary sorting.

Only one example has been cited from among the large volume of research and organizational work directed at improving methods for the timely detection of malignant tumours in patients.

Prophylactic examinations using different methods are conducted by physicians in all specialities, but diagnostics and treatment should be the task of oncologists. It is no less difficult to establish an exact oncological diagnosis than to unravel a mysterious and complicated crime. The analogy is very fitting because many case histories (if viewed by a writer like Simenon) are like detective stories about real tragedies. The main actor in these tragedies is, of course, the patient, but his relatives, the doctors and the medical personnel also play important role. The disease snatches a person from his habitual life and throws him into a hospital bed. The psychological aspects of the disease shall be examined in a separate chapter, but what follows is a brief discussion about making diagnostics more precise.

In *Doctor Krupov* the writer A.I. Herzen remarked that a doctor must not judge an object simply by its appearance; as a result of such an approach the whale was for a long time considered to be a fish. Before all else, one must make sure that a specific hardening, or ulcer, is of a tumoral and not of some other nature.

Confirmation of the presence of a malignant neoplasm is not the final stage of diagnosis, but only the beginning, since the question of the possibility of treatment, choice of method, etc. may be decided on only after a thorough examination has been made of the patient and of the tumour.

It is essential to determine the organ that is afflicted, and the exact location of the tumour in the organ, because carcinoma of the cardiac part of the stomach or of the pyloric part require absolutely different operations. This is true for many localizations of carcinoma.

Further, the oncologist is obliged to know the degree to which the process has spread, because the growth of the tumour and its penetration into neighbouring tissues and organs requires maximum extension of the operation. Subsequently, another stage may develop when surgical intervention is either useless, or more hazardous than the disease itself. These same circumstances may dictate the need to resort to additional methods of treatment such as radiation and chemotherapy.

As for the specific characteristics of the tumour, the less differentiated it is, i.e., the further it has developed structurally from the initial tissue, the less successful will be the operation. It is therefore customary to distinguish surgical tumours, for which the operation promises success, and therapeutic tumours where an operation will hardly help and it becomes necessary to try conservative methods of treatment.

Dozens of methods have been currently developed in research establishments; these are methods that make it easier for the oncologist to diagnose the disease.

At the P.A. Herzen Institute, even in the case of such an "accessible" tumour as breast cancer, in addition to detailed questioning of the patient, examination and palpation, comprehensive control tests are applied as a rule. This includes roentgenography of the gland, the infusion of a contrast medium into the lactic ducts followed by X-ray examination, a study of the lungs by X-ray, the infusion of contrast substances into the vein of the thoracic wall to obtain its X-ray picture, analysis of the tumour absorption of radioactive isotopes, puncture with a fine needle for taking "samples" of cells, and investigating the hormones of the patient. If all these methods nonetheless fail to fully disclose the nature of the process, a diagnostic operation is performed with removal of part of the gland and immediate histological analysis of the tumour.

A careful comparison of all the data makes it possible for the oncologist or, as is the rule in the USSR, a consultation of specialists, consisting of a surgeon, radiation therapist and a specialist in drug therapy, to work out a reasonable plan in which the surgery is generally a stage, an important and at times the most complicated stage, but nonetheless only a stage of multicomponent treatment.

The specific character of medicine is such that not all questions, whether they concern the diagnosis of the disease, choice of treatment or surgical method, the possible outcome, etc., can be decided simply. Medicine, as yet, is not a precise science although medical publications are filled more and more with mathematical formulas and discussions about algorithms. During a lecture delivered at the turn of this century, the famous Russian surgeon S.I. Spasokukotsky joked that it is easy to convince students that one cannot be a good physician without a knowledge of integrals and differential equations, but nowadays one can say quite seriously that such a time is near. At this time, however, very much still depends on the personal experience of the physician, the level of his knowledge and his knack for correctly assessing important details.

This to a great extent explains why medicine, more than any other sphere of human activities, lends itself to a system of mutual consultation and discussion. This is particularly true when the matter concerns cancer patients, the diagnoses and treatment of whom often present considerable difficulties.

This is very convincingly and accurately described by Arthur Hailey in his novel *The Final Diagnosis*, which is about everyday life and work in a large American hospital. In the novel, physicians suspect that Vivien, a young student in a nursing school, has sarcoma of the leg. The radiologists are unable to explain the nature of the tumour; whether to amputate the limb or not depends on an answer. The right to decide such a crucial question belongs to the morphologists, because the morphological method is considered to be the most objective and reliable one in oncology. This, of course, is not because the physician's decision is not influenced by the personality of the patient whom he has most likely never seen. Hailey shows that when studying a specimen the doctor cannot but think about the fate of the suffering patient.

In connection with this, it is interesting to learn how Z.V. Golbert, one of the most experienced Soviet morphologists in the country, examines histological specimens. Professor Golbert headed the Pathomorphological Department of the Herzen Oncological Institute for many years. Even now, despite her venerable age, she is a constant visitor to the laboratory helping her pupils analyze some of the most complicated diagnoses.

Professor Golbert first examines the glass covered with film held against the light with the naked eye. In all probability at this stage this most experienced specialist already forms an opinion about the intensity of the tissue colour and the quality of the specimen. She will never offer a conclusion if the preparation is bad (either too thick or over-dyed). When looking through the microscope she becomes very excited:

"Just look!" she exclaims, "What ugly, awful cells! They are pushing aside the healthy ones and clambering through their layers. Do you see? There's one very evil cell that has wormed its way into a position where it has absolutely no right to be!"

"Professor! I see nothing!"

"Look properly through the microscope!"

She herself seems glued to the instrument, adjusting the focus rapidly, increasing the power of the magnifier.

"Look, what an ugly cell! It is most frightening to see! You must destroy that vile abominable thing! It is a very dangerous form!"

She slides the form nearer to write her conclusion.

The decisive importance of the morphological method in establishing a final diagnosis is connected with the fact that through the microscope the physician is able to discern the principal signs of malignant growth. This takes into account not only the "appearance" of individual cells, which in cancer are distinguished by their peculiar shape, colour, and intensified division, but also by the mutual position of the cells, the correlation of cellular layers. Special attention is focussed on the borderline between tumour cells and normal tissue. The penetration of cells through bordering membranes testifies to the malignancy of the process.

Even such a precise method, however, is not entirely objective. Evidence of this are the results published in a foreign medical journal of a parallel histological investigation of the same specimens of primary cervical carcinoma carried out by several experienced pathologists. Here, all the histologists have the same unambiguous answers for only 10 per cent of the specimens. The diagnoses of the remaining specimens ranged from normal to an advanced stage of cancer. This is why in questionable cases, morphologists also resort to consultations.

In Hailey's novel the consultation of morphologists pronounced the merciless sentence.

If the writer were telling his story today he might have saved the unlucky girl her leg, because most recently physicians have begun performing operations that replace the affected bone with a special transplant.

Treatment, however, is the topic of the next chapter of the book.

The Statistics of Survival

This chapter, which is about the treatment of malignant tumours, is introduced with a statement from an article written by P.A. Herzen: "The diagnosis of cancer affects the psychology of the patient and the doctor so severely that it immediately evokes the most drastic action—cut it out, burn it out, destroy it!"

That was the reaction 50 years ago when P.A. Herzen wrote his article. The same feelings overwhelm all those concerned today! To cut it out, burn it out, destroy it!

The first and for a long time the only method for ridding a patient of cancer was to remove the tumour with a knife or to burn it with a red-hot iron. Before the end of the last century it was practically impossible to find any report in the medical literature about a stable and reliable cure for malignant tumours (when the diagnosis of cancer had been confirmed by morphological investigation). The poor results, as we now realize, were to a great measure due to the fact that the operated area most often passed near the tumour but failed to include the organ's lymph nodes, which the metastases tended to invade first.

A fundamental turning point occurred when in 1896 the famous surgeon Halsted extended the boundaries of the operation for breast cancer; he proposed removing the entire organ together with the thoracic muscles and the lymph nodes contained in the armpits. Halsted's initial intention was to alleviate the suffering of women with a disintegrating tumour, but follow-up observations revealed that some of the patients were permanently cured. Moreover, nearly half of the patients with small tumours recovered after Halsted's operation. After these results, operations following the same principle began to be performed on other malignant neoplasms.

An oncological surgical operation is usually very complicated and calls for the observance of specific rules. It is insufficient to remove just the tumour or the afflicted organ. It is essential to skillfully attend to all the surrounding tissues and lymphatic ducts. In doing so, however, one must be careful not to "disperse" the cells, each of which may become the source of a new malignant growth. Just as in asepsis (preventing infection of the surgical wound with microorganisms), a new term was introduced, "ablastics", which is measures preventing cancerous cells to be dispersed or left in the organism.

In 1901 M. Lakhtin published a book entitled *Great Operations in the History of Surgery*. The operations that were considered "great" at that time were blood-letting, perstriction of vessels, cranial trepanation, limb amputation, Caesarean section and a few others. They hardly seem stunning to the imagination today; even a beginning surgeon can perform such operations. It would be more proper to call operations such as amputation "crippling operations".

The rapid development of surgery is connected with the discovery of methods preventing wound infections, the use of anaesthesia, and the transfusion of blood and blood substitutes. All these breakthroughs made surgical operations possible on vital areas of the human body. The brilliant successes of modern surgery were first used in oncology. The surgical treatment of carcinomas of the stomach, oesophagus, intestines and lungs have now become routine for any skilled surgeon on the staff of qualified oncological hospitals.

It would seem that the surgical method for removing tumours described above would be invincible, but the voices of skeptics are becoming louder and louder. The scepticism concerns the theoretical conception of the operation as being exclusively local. Thus, the late Academician R.E. Kavetsky held the opinion that "The task of surgical treatment lies in removing all tumour cells from the organism, but it has long become clear that this is impossible and that the fate of the remaining tumour cells depends on the condition of the organism." Professor Frank Rauscher, Vice-President of the American Cancer Society, is in agreement with this. He believes that the surgical treatment of cancer does not hold much promise, because in 60 per cent of the patients, by the time they consult a doctor, the tumour has already spread widely. According to the eminent Soviet chemotherapist Professor A.M. Garin, the indisputable surgical successes during the early stages of cancer can be explained by "the quantitative interaction between the tumour cells remaining in the organism after surgery and the immune lymphocytes, in favour of the latter. Thus, with some reservations, surgery may be called a method for the immunotherapy of tumours." After such reasoning the obvious conclusion to be made is that, with progress in science, the importance of surgery in oncology will be sharply reduced. It is quite possible that it will no longer exist, having surrendered to more radical, but less traumatic, methods of treatment.

It is not the first time that this subject has been raised. One of the most heated discussions was held approximately half a century ago. It should be described, for, as a historical interpolation, it will help to clarify what is happening today.

The polemics were sparked off by the article "Surgery at the Crossroads" written by Professor S.P. Fedorov in 1926. In the Russian medical literature there were not many publications that gave rise to such a lively discussion and animated exchange of opinions as this article. In uncompromising analysis, polemic ardour and literary skill it was akin to Veresayev's *Notes of a Doctor* which had captured public interest about 25 years prior to this publication.

The author of this article was an outstanding surgeon comparable in stature to N.I. Pirogov. He lived the greater part of his life before the Great October Socialist Revolution and could not properly evaluate its historical role when it took place. A former attending surgeon at the court of Tsar Nicolas II, he was twice arrested by the Petrograd Cheka (Committee Extraordinary) for illegal connections with White Russian émigré, but eventually released when Maxim Gorky intervened on his behalf with the support of the Russian N.I. Pirogov Surgeons' Society. During the investigation and at the trial Fedorov confessed that he had been assiduously urged to go abroad, following the example of some of his colleagues who were professors of the Military Medical Academy, but he had categorically refused to leave the country. The democratic sentiments of this outwardly haughty general, who had a neatly trimmed aristocratic beard and arrogant mustache accentuated by a constant cigar in his mouth, often won over. For example, when a new medical journal was first published, he called on the editors to "keep pace with the provincial medics" because he considered many of them to be highly professional in surgery.

Soon after 1917 Fedorov saw that the revolution was a powerful impetus for the development of all the productive forces of the country, as well as of science, and became actively involved in the development of socialism. His dedication to this effort was evidenced by the fact that this former tsarist official was the first surgeon to be honoured with the highest order of his Motherland—the Order of Lenin—for his outstanding achievements in surgery and in training cadres of physicians for the Workers' and Peasants' Red Army.

His scientific and clinical interests embraced practically all branches of surgery, in each of which he left an indelible heritage, founding his own school and initiating original trends in its development.

All this heightened the interest in Fedorov's article. Here was an eminent scientist who, from the height of his prestige and position, was openly critical of the direction in which surgery had been developing. In evaluating its splendid past due to the merits of aseptic techniques and anaesthesia, Fedorov asserted that he perceived no other possibilities in the future that could stimulate such unrestrained development in surgery.

Time has proven that the article, which was written during a period of doubt and uncertainty, contained many erroneous conceptions (such as a negative attitude to the narrow specialization of physicians, a skeptical opinion of the scientific interests of young colleagues, and the sweeping rejection of new surgical methods). Nevertheless, his article gave public opinion a jolt and made surgeons ponder over the philosophical essence of their scientific and clinical activities.

The yellowed pages of old medical journals reporting on the discussions that were held at the time are as interesting today as novels because they are saturated with the reflections and ideas of people who possessed vast clinical experience. Prominent among other views voiced at the time are the opinions of Professor P.A. Herzen.

In 1927, in the magazine *Vestnik Sovremennoi Meditsyny* P.A. Herzen published an extensive polemical article entitled "The Urgent Tasks of Surgery". In this work, which is, to a great measure, a philosophical treatise, it is easy to trace a connection to the view held by A.I. Herzen on skepticism. These opinions are expressed in his book *From the Other Shore* as well as in the story *The Doctor*, *the Dying and Dead*, where he illustrates that skepticism, even if enriched by knowledge, may lead one up a blind alley if one does not seek ways for active intervention in life.

Fully realizing this, P.A. Herzen tried to help surgeons out of such a dead end.

The reader can see that this article was written in a single burst of energy, that it was truly a subject that the author had actually suffered for. From the first to the last sentence, the text is imbued with optimism.

P.A. Herzen argues with those specialists who contend that prophylactic measures may "nullify" surgery. Without naming the initiator of the discussion, whom P.A. Herzen deeply admired, he thoroughly tore apart Fedorov's article, asseverating that "it is only a few surgeons who stand perplexed at the crossroads, but not surgery itself...".

P.A. Herzen underscored the mounting, never-ceasing consolidation of the scientific and material basis of surgery, the refinement of techniques and the increasing number of lives that were being saved. "If such are the facts, then where is the crisis in surgery? Is it really at the crossroads, uncertain which direction to take?" he asks.

Herzen was against the view that the surgical method should be restricted because the organism is left with a defect.

"...It would be hard to imagine Apollo... without a prostate, with just half a stomach, without a sympathetic nerve in his neck, with a trephined mastoid process (of the temporal bone) or a damaged iris due to a cataract, without teeth, and so on," jokes Herzen; but he turns serious as he reminds the reader that the surgeon does not operate on a healthy person, but on a patient who has lost his working capacity.

One of the most vulnerable points in Fedorov's article concerns the role of surgery in oncology. "When I was young," Fedorov used to say, "I was more or less sure that recurrences of malignant tumours occur because the surgeon lacked sufficient skill to perform a radical operation... On gaining a certain measure of independence, I decided to 'show' how an operation should be performed.

"It was evident that nothing could become of this. Experience ultimately proved that the crux of the matter is not in the scope of surgical intervention; this is only one of the minor ingredients.

"Breast cancer demonstrates this clearly: after an extensive and well-executed operation performed even at an early stage of the disease, a recurrence frequently occurs earlier than following a poor operation performed at a later stage. Resection of the oesophagus, of the entrance to the stomach (cardia) has yielded nothing but a terrible mortality rate. And I myself have been a bit involved in this matter..."

In reply to Fedorov, presenting as proof of his case the data accumulated from his wealth of experience, P.A. Herzen affirms that cancer at the beginning of its development is a local process that is quite curable by timely surgery. Thanks to this type of surgery, there are between 35 and 65 per cent recoveries in breast cancer, and between 50 and 90 per cent in carcinoma of the lower lip. The failures in treating cancer of the internal organs are due to the difficulties in early diagnosis, and not to a crisis in surgery.

Both these statements need to be commented on from the contemporary point of view.

Fedorov correctly noted that the outcome of the treatment of malignant neoplasms depends not only on the surgeon and the method of operation, as he had so vainly first believed when he was still a very young doctor. Certainly, the prognosis is influenced by the stage of the disease process, the degree of the tumour's maturity, and the resistance of the organism.

Therefore, in the early stage when, as P.A. Herzen puts it, the tumour is still "a local pathological change", there are more chances that good results will be produced by a skilfully performed operation than when there is a large tumour that has spread beyond the diseased organ. There can hardly be any guarantee that the surgeon will be able to remove all the cancerous cells which may become the embryos of new tumorous growths.

In exactly the same way, under equal conditions, the treatment of mature tumours is much more promising than that of undifferentiated tumours which behave particularly wickedly. They rapidly grow, quickly penetrate surrounding tissues and produce early metastases. In many cases of such tumours surgical intervention must be rejected and other methods tried.

In determining the components upon which the prognosis depends, however, one must never underestimate the significance of surgery as Fedorov does. The illustration which he chose as an example does not produce adequate consequences in treating breast cancer: a good operation in an early stage is less effective than a poorly performed operation at a later stage.

Is such a situation possible?

To reply to this question, the terms must be more clearly defined. The term "recurrence" after the radical removal of the tumour is usually understood in oncology to be its reappearance at the place where it had been before. In speaking about a recurrence Fedorov evidently had a wider concept in mind, i.e., the relapse of the disease, including the appearance of "daughter" foci of the tumour (metastases) at some distance from the initial site. At the same time the source of the metastases can only be tumorous elements which had spread prior to the operation but until a certain moment had given no sign of their presence.

In oncology the true radical nature of surgical intervention is not determined immediately, but only after some time has passed because the "traces" of cancer cells which may remain begin to behave as metastases usually during the first two years. With the passing of time following surgery, the probability of recovery increases, and after five years, as has been mentioned, the disease practically never recurs.

Large tumours metastasize more often, but sometimes, remote metastases may also occur with small tumours. It is this small percentage that accounts for the failures of radical treatment during early stages of breast cancer.

The very essence of the question consists in the fact that the conception of cancer as a general systemic disease is by no means axiomatic. Malignant neoplasms are presumed to be "solid" tumours stemming from some concrete organ or tissue (stomach, lung, mammary gland, etc.) and "systemic affections" are those that embrace an entire system such as the lymphatic (lymphoma, reticulosarcoma) or the haemopoietic (leukoses and others) systems. Strictly speaking, any malignant disease consists of both local affection and an overall reaction of the organism.

The overwhelming majority (80-85 per cent) of solid tumours for a long time retain the character of mainly a local process, and in only 15 to 20 per cent of the cases they are aggressive from the very beginning. This question has not been studied thoroughly as yet and there are no criteria for discerning tumours with primarily local growth and those that are primarily metastasizing. Some distinctions were made in electron-macroscopic investigations conducted by N. Raikhlin and A. Yagubov. The outstanding Soviet X-ray specialist S.Ya. Marmorshtein demonstrated that cancer of the lung grows no less than between 5-7 years before it shows clear clinical signs, i.e., before the stage of metastasis. Consequently, in solid tumours as long as they remain "in place", even a comparatively minor operation may result in full recovery. This is exactly what happens in reality. In his reply to Fedorov, Herzen mentioned the percentage of recoveries in breast cancer to be between 35 and 65. The results today are far more impressive: as has already been noted, health is restored to 90 per cent of female patients in the first stage of the disease.

Just over fifty years ago Professor A.M. Zabludovsky, a Leningrad surgeon, published an article entitled "Is it necessary to operate carcinoma of the stomach? If it is necessary, when should the operation be performed?". The title may seem odd to us today but the work reflects the author's pessimistic views on this problem. For a long time now, the problem has not been presented in such a manner, because surgical treatment for carcinoma of the stomach produces a stable positive effect in up to 40 per cent of cases, and even more when caught in the early stage of the disease.

Concerning complicated surgery that requires entering the stomach, which Fedorov considered to hold no promise whatsoever, data collected by Professor B.E. Peterson reveal that every third patient undergoing such a radical operation is successfully cured.

There is a reason for making the stipulation "undergoing a radical operation" because, unfortunately, many people are not operated on until the disease has reached an advanced stage, either because some patients refuse to be operated on or because of general contraindications.

Old age is often attended by a variety of serious diseases of the cardiovascular, respiratory or endocrine systems. As a rule, our patients are well-advanced in years. One female patient defined her age in the following way: "When my apartment was under repair and some old newspapers were thrown on the floor to keep it from being spoiled, I read that Peter the Great's 300th birth anniversary was being celebrated, and I remembered that, when I was in high school, we also celebrated the 200th anniversary of the battle of Poltava."

In recent years, indications for operating on patients with aggravated conditions have increased (with the exception of spread cancer, which holds no promise for recovery). The accomplishments of gerontology, therapy and anaesthesiology make it possible to perform operations more often on elderly people suffering from attendant diseases. Any experienced oncological surgeon is sure to have patients who although they are more than seventy or eighty years of age, have successfully undergone serious operations for cancer. (One cannot help but recall that at the beginning of this century Chekhov stated, through the words of Dr. Dorn, the hero of his play *the Seagull*, the following: "Treatment, not surgery, but ordinary therapeutic treatment should at 60 years of age be considered a very frivolous thing.")

Today, the patient's age, as such, is no barrier for surgical treatment.

A consultation of specialists, consisting of an oncological surgeon, an anaesthesiologist and a therapist, meets practically every day to weigh the "pros" and "cons" for surgical intervention. But where are the scales on which the risk can be weighed with necessary precision? Unfortunately, there are no such scales, but there are experience, intuition, skill and the earnest desire to help the patient. We always bear in mind P.A. Herzen's injunction that we have no right "to be brave at somebody else's expense".

Oncology originated in the bowels of surgery. The appearance of gamma-therapy in its time, and particularly, the fortunate therapeutic effect on certain forms of malignant tumours gave physicians hope that surgery would yield its position, but this did not happen. There is no sign of the gradual "waning" of the surgical method; on the contrary, it is more and more often the only method of treatment. In Moscow, for example, the number of cancer patients who underwent surgery with no additional anti-tumoral treatment increased by over 10 per cent in the last ten years. This was mainly due to the improvement in the diagnosis of cancer, of its primary forms. In "minor" cancer, surgeons can already deviate from the canons of oncology and perform organ-saving operations that had only recently been strictly forbidden. There is an increased percentage of operations, for example, which leave the pulmonary tissue on the side of the affected area untouched. This tissue immediately, right there on the operating table, becomes involved in the process of respiration and gas metabolism, which helps the patients to overcome the trauma more easily. The introduction of such operations in practice has expanded the possibilities for surgical treatment of lung cancer primarily in elderly and weakened people with insufficient heart-and-lung reserves.

The development of the functional approach in oncology is especially noticeable in the changing character of reports and demonstrations presented at meetings of the Scientific Oncological Society of Moscow and the Moscow Region. The time has passed when the results of super-extensive, large-scale operations were demonstrated. At that time one was amazed not only by the skill of the surgeon but also by the endurance of the patient. Today, more importance is attached to organ-preserving operations (without diminishing their radical nature).

At working sessions of the Society one rarely hears applause nowadays, like those that occurred when a group of patients presented by N.E. Makhson, D.Sc. (Med.), performed various physical exercises: a female patient whose leg would have formerly been amputated at the hip joint due to the character of the tumoral process, now squatted easily; a young man whose arm would have been amputated along with his shoulder blade, now boxed with agility.

Although not as impressive, organ-preserving operations on the rectum, urinary bladder and larynx are also of vital importance for patients.

Let us not delve into the depths of surgery, however, lest the same thing happens as when a young doctor came to watch an operation for cancer of the head of the pancreas performed by one of the authors of this book. The young man was attending an advanced course for physicians and the operation he witnessed lasted four hours. (A typical symptom of this disease is mechanical jaundice with the skin and sclera of the patient turning yellow.) After the surgeon had explained all the details of the operation to the observing student, for the four hours that he worked, he asked the young doctor if the surgical procedure had been clear. The latter nodded, took a look at the yellow colour of the patient's skin and asked just one question: "Please tell me why the patient has to be entirely painted with iodine?"

Let us discuss the new methods of surgery.

The local freezing of tissues—cryosurgery—has received recognition by clinical practice in recent years. Cold destroys the tumour and it is replaced by connective tissue. At the same time a tender superficial scar is formed. Cryosurgical operations are particularly justified in tumours affecting the skin of the face, when the application of the scalpel may cause cosmetic defects, and also when access with the scalpel is difficult, such as in affections of the acoustic meatus.

The best results are actually achieved with quantum generators, i.e., lasers. The laser acts on biological targets with a flash of unprecedented power, causing peculiar changes in the tissues which resemble thermal burns. In principle, the basic advantages to using lasers in oncology are its lightning-fast impulse, the high selectivity for pigmentary structures, the increased sensitivity of tumours to radiation, the bloodless and painless procedures, and the minimal side effects on the surrounding normal tissues and the rest of the body.

Long years of intensive labour go into perfecting every surgical method and this work is no less absorbing than developing the theoretical foundations of oncology. It is most gratifying to note that in 1981 the State Prize of the USSR was conferred upon a group of scientists (O.K. Skobelkin, S.D. Pletnev, V.P. Bashilov and others) for their introduction of lasers into surgical and oncological practice.

We already mentioned the year 1896, which proved to be so fortunate for oncology: in this year Halsted proposed an operation for breast cancer that became a model for other operations. That same year just a few months after Röntgen discovered penetrating rays, an attempt was made to treat cancer by radiation, a method which soon came into its own as another classic treatment for malignant tumours. It should be added that in 1896, Anri Becquerel, a professor of physics at the History Museum in Paris, discovered the phenomenon of radioactivity, thus "prompting" Marie and Pierre Curie in their search for radium.

The beginning of the 20th century coincided with a new era in the offensive launched against cancer. The annals of Soviet roentgenology and radiology began with the victory of the October Revolution. Even during the period when the country was undergoing its severest trials—the Civil War and devastating ruin—the Soviet Government spared no expense for the development of fundamental research. In 1919, at the initiative of Professor M.I. Nemenov, and with the active participation of A.V. Lunacharsky, the Petrograd Roentgenoradiological Institute was founded, this was the first specialized scientific institution of its kind in the world. Later, similar establishments were organized in Kiev, Kharkov, Moscow and other cities.

There is no other branch of medicine which depends to such an extent on physics, technology and methodology as radiation therapy. Today, X-rays are used very rarely in medical treatment; they have been replaced by far more powerful sources of radiation of electromagnetic and corpuscular nature.

For the benefit of those readers who have long finished school and forgotten their physics, corpuscular radiation consists of a flow of elementary particles—electrons, positrons, neutrons, deuterons and alpha-particles. Electromagnetic X-ray and gamma-radiation are the flow of quantums lacking a charge, the energy of which is determined by the physical characteristics of the wave (frequency, length). Both kinds of electromagnetic radiation travel in a vacuum with the velocity of light.

In all probability, the essential biological effect of all the variants of radiation therapy is identical, namely, the emission of elementary particles from the nucleus of the radioactive isotope and their absorption by cells and tissues is accompanied by gamma-radiation. The great variety of radiation sources, however, predetermines the truly boundless possibilities for varying the doses and methods for directing them to the target with minimal radiation damage to the surrounding space. The natural radioactive substances (radium and mesothorium) are currently not used for this, but are replaced by artificial substances that are much cheaper and, most importantly, more selective in treatment. For example, the radioactive alloy of cobalt and nickel is used to make needles, threads, beads and so on, which are positioned at strategic spots for contact irradiation of tumours. An artificial isotope of gold is used in the form of a colloid solution introduced into the abdominal and pleural cavities. A liquid solution of the radioactive isotope of iodine can be infused intravenously: it is capable of "locating" metastases of carcinoma of the thyroid and of actively attacking them. The "ancient" radioactive cannons have been replaced by devices that very precisely observe dosages and can outline fields of exposure to radiation of any general shape. Patients are treated by an accelerated flow of electrons, protons and so on.

Although many decades have passed

since the first application of radiation therapy in oncology and the results have been very impressive, it is still not fully clear what the biological effect of ionizing radiation consists of. This is yet another of the paradoxes of modern science and again we are convinced that the lack of complete understanding is no barrier to the improvement of practical applications.

What is actually known?

Radiation energy suppresses the capacity of tissues for restoration (scientifically known as regeneration) at the expense of inhibiting the growth and reproduction of cells. This, of course, is true for specific doses; if the doses are too large, the cells will simply be killed without any “concern” as to whether or not they are needed by or harmful to the organism. If all the cells and tissues reacted to irradiation in the same way, radiation therapy would be impossible. Fortunately, this is not so. Depending on a number of biological characteristics of the “target”, the results of exposure to radiation are very different.

Let us review what makes a tumour cell different from a normal cell. Basically, it is the rate at which it divides. The reaction to irradiation depends precisely on this property: the greater the tissue's ability to reproduce, the faster the cells divide, and the more sensitive they are. Unfortunately, these same tissues have an increased capacity for regeneration. This is why it is difficult to expect results from one exposure to radiation. Treatment has to be repeated many times.

There is a ruse which allows a weak individual to move or even topple a strong man, no matter how steady the latter seems to be on his feet. The secret lies in rapid and rhythmic, but light, jabs to the upper half of the trunk. Such repetitious painless hits are far more effective than one powerful push. Outwardly the same is true of radiation therapy.

The usefulness of radiation therapy depends on the skill of the radiologist just as much as the outcome of an operation depends on the skill of the surgeon. The radiologist, based on the data of the patient's examination, and the location and the morphological characteristics of the tumour, chooses the source of radiation emission, the optimal dose, and the means by which it is directed at the target, including the rate, length of intervals, etc. Such a multifactor analysis is a standard task for a computer. This is why miniature computers are currently in wide use at many leading radiological centres, greatly aiding specialists.

Unfortunately, not every form of cancer is sensitive to radiation therapy. Nevertheless, oncologists manage to completely "eliminate" quite a number of tumours by this method, skillfully combining different variants. Successful treatment of specific stages of cancer of the cervix, the skin, tongue, lips, etc., has been achieved.

A graphic illustration of the as yet uncovered possibilities of radiation therapy is seen in the evolution of the tactics employed in treating lymphogranulomatosis. The tendency in the last ten years has been to conform to the so-called radical programme: the zone of intensive radiation, besides the obvious foci of affection, includes all the lymph collectors above and below the diaphragm. The positive results are obvious; until quite recently no more than 10 per cent of patients who had been treated at stages I and II of lymphogranulomatosis were expected to survive five years after treatment, whereas now 80 to 85 per cent of the patients survive, 60 to 70 per cent survive up to ten years. This constitutes an immense success.

In the Soviet Union, radiation therapy alone, as the only radical method, is undergone by every third patient suffering from a malignant tumour. Of even greater importance is its use in combination with other methods. Such a need arises practically every time a patient rushes to a doctor long after he should have; in this case the tumour has already spread beyond the initial organ and one operation or radiation treatment alone is already insufficient to save the patient's life. This type of treatment is used to fight the tumour that develops in carcinoma of the thyroid gland.

For example, imagine that part of the thyroid gland in a young man begins to increase in size rapidly and he begins to feel very sick. Examination establishes cancer with metastases in the lymph nodes of the neck and both lungs. This form occurs fairly often in young patients. Twenty years ago such a formidable diagnosis would have spelled death, but now the patient undergoes radiation therapy with an apparatus which contains a considerable dose of radioactive cobalt in its head. An intricate system of devices makes it possible to shape the field of radiation and regulate doses in such a way that practically the entire beam is directed at the tumour, while the healthy tissues of the strong organism are almost not at all harmed. When the tumour and metastases diminish considerably and their biological activity is reduced, the thyroid gland and the lymph nodes in the neck are removed. As soon as the patient recovers from the operation, he is returned to the radiological ward and radioactive iodine is infused. It was mentioned that this substance selectively accumulates in the lung metastases which retained the vital property of the thyroid gland to "attract" iodine. Since the radioactive isotope of iodine is "absorbed" by the metastases, activity is concentrated there, which proves sufficient to destroy the remnants of the tumour. Whenever necessary the procedure is repeated regularly.

According to data from the P.A. Herzen Institute, combined treatment of even such a severe tumoral condition gives two-thirds of the patients a chance to live and work for another 5-10 years and even longer. There are patients who are observed to be in good health for more than 20 years.

Another interesting example is the following: at the last congress about cancer held in Argentina, one of the delegates described his experience in treating advanced forms of lung cancer. The surgeon opens the patient's chest and if he finds that it is impossible to remove the tumour, he invites a radiologist to the operating room. The latter introduces special radioactive wires into the tumour. After some time another operation is performed and sometimes the tumour, which has sharply diminished in size, can technically be ablated. The author of the report confirmed the fact that patients who had been operated on in this way have already survived for five years.

Why, then haven't all cancer patients with inaccessible tumours been treated in this manner? This is because not every tumour is equally susceptible to the effects of radiation. The problem is that the general pattern whereby the effect depends on the rate of cell division is not absolute and there are many other attendant circumstances which seriously influence results. Moreover, the sensitivity threshold of the tumour and of the healthy tissues is often infinitesimal and the dosage that should destroy the tumour may actually harm the surrounding area, including parts which are vital for life. There exists the danger of killing the patient in the attempt to destroy the tumour. Several generations of scientists have been tackling this difficult problem.

In 1909 the German X-ray specialist Schwartz noticed that if the skin is squeezed, thereby limiting the blood circulation in the area, the sensitivity to irradiation weakens and doses may be increased without causing any substantial harm. It was further established that changes in the saturation of tissues with oxygen by various means, including a reduction in circulation, have quite a different effect on the radiation sensitivity of tumour cells and healthy cells. This opened up opportunities for future clinical application. In the Soviet Union, this possibility was given wide application at the P.A. Herzen Institute in Moscow.

Radiologists used two approaches: (1) prior to and during irradiation the patient is placed for some time in a pressure chamber where the oxygen pressure has been increased up to three atmospheres; (2) if the patient's extremities are swollen ligation is performed prior to irradiation so as to limit blood circulation.

In the first case the oxygen exchange in the tumour changed very noticeably and the tumour became more susceptible to ionizing radiation. In the second case the resistance of unaffected tissues grew and it became possible to increase the dosage considerably. In both cases promising results were produced, particularly in some forms of lung cancer and sarcomas of the limbs.

The most curious result was that this experiment with radiation therapy in a pressure chamber proved to be useful for increasing the efficacy and reducing the toxicity of certain drugs used in oncology. Moreover, scientists discovered chemical substances which stimulated the radiosensitivity of tumours, namely, radiosensitizers. With the help of these agents chemoradiation treatment was organized which is now recognized universally. On the other hand, in experiments on animals, chemical substances that protect normal tissues from the penetration of rays were discovered; they are called radioprotectors. In-depth research is currently being conducted for introducing radioprotectors into clinical practice.

Sometimes the effect of radiation therapy can be increased by seemingly simple devices which provide for a more exact "delivery" of energy to the target. This also decreases the hazards involved for personnel working in radiology departments. Small hollow pipes specially made for this purpose are aimed at the affected areas and secured in this position. X-ray control keeps these devices properly adjusted. The patient is placed in a specially protected ward where he is bombarded for 2-3 seconds by active agents passing through these pipes. This treatment effects cures in the clinic in 91.4 per cent of cases of carcinoma of the cervix, for example, while cases of complications due to irradiation are reduced by three to four times. Since many stages of radioactively hazardous work are excluded, the total dose of radiation exposure received by the medical personnel is decreased fivefold.

Scientists have not given up seeking new sources of radiation therapy and are expanding the sphere of application of protons and neutrons. Much concern is shown for designing apparatuses for remote-control gamma-irradiation, the use of linear accelerators of electrons and betatrons. Radiobiology is developing and setting new tasks for clinical medicine. The ability of radioactive iodine to accumulate selectively in the cancer metastases of the thyroid gland prompted scientists to try to discover other isotopes which would strive to reach specific organs. It is possible that they could even help to transport effective anti-tumoral agents to areas of affection. At the present time diagnostics is exploiting ability of radioactive gold to concentrate in the liver and spleen, of radioactive strontium and technetium, in the bones, and so on. This task is quite feasible. Radiation therapy has always been and remains one of the most effective means for preventing the growth of malignant neoplasms.

We again wish to underscore that the achievements of the surgical and radiation methods of treatment would be much greater if cancer patients appealed to doctors when the disease was only in the first or second stage of development and there existed a real possibility to cure the local tumour. After radiation therapy alone in the early stages of the disease 95 per cent of the patients suffering from cancer of the skin survived for another five years; between 80 and 90 per cent survived after cancer of the cervix; 85 per cent, after cancer of the larynx; 55 per cent, after cancer of the thyroid gland; 45 per cent, after cancer of the tongue; etc. If the tumour grows into the surrounding organs or if it begins to metastasize, neither the surgeon's scalpel, nor a flow of energy, nor a laser beam can keep the "spreading" complexes of cells in check as they rapidly develop into new sources of cancer. During irradiation even the complete reverse development of the disease gives no assurance for recovery if the anatomical position of the irradiated target does not allow the necessary dosage of radiation to reach it. In addition, the manipulations of the surgeon on the organ affected by the tumour may complicate the "squeezing out" of tumour cells that are swept away by the flow of blood.

The fundamental flaws of the two basic methods of treatment are overcome when they are combined. This has already been mentioned. Recently, surgery and radiation treatment have been supplemented by chemotherapy and hormonal treatment.

Chemotherapy appeared almost 40 years ago and the first anti-tumoral agent was embichin, a derivative of mustard gas (yperite), a poisonous gas used by Germany in chemical warfare during World War One against the British troops at Ypres.

The World War Two was in progress. The fascists were expected to resort to chemical warfare at any moment. And Goodman and Gilman were American researchers who, while studying the effect of certain derivatives of yperite, noted their inhibiting influence over lymphoid tissue and rapidly dividing cells. The idea was expressed that it might be expedient to test these substances on tumours, i.e., in lymphogranulomatosis. The assumption of the scientists proved justified. The Soviet analog of embichin, novoembichin, derived at the beginning of the fifties by Academician M.F. Larionov, also proved effective in general affection of the lymphatic system.

The first successes were scored by curing a large group of patients who had been suffering from what had earlier been considered mortal forms of malignant diseases. This gave rise to hopes and a new trend was thus started in experimental and clinical oncology. Already in 1962 the WHO Committee declared that chemotherapy was confronted with a task of immeasurable difficulty: it was necessary to learn how to destroy all the cells of a great variety of tumours without causing any harm to any of the healthy tissues which in their biochemical composition (not counting certain quantitative differences) were not fundamentally different. This task reminds one of the radiation method.

Our distant forefathers, in their search for medicinal herbs tried everything that happened to be at hand, testing on themselves the pharmacological properties of the nature around them. This was a primitive method and it was later "improved" by experiments on animals, but the tactic of "trying out" all the candidates for medicinal agents remained. The German biochemist Paul Ehrlich labelled the antisyphilitic agent he discovered in 1907 salvarsane No. 606, recording all his efforts in this way for the sake of history until he achieved success. If anybody in our time would decide to number the sample tests of any of the 50 or 60 existing anti-tumoral chemical agents, the number would require many added zeroes.

B. Glemser cites the following figures to characterize the scale on which this search is being conducted: in the United States during one decade, 257 000 different substances were tested for anti-tumoral activity, the money spent on this research totalled over 250 million dollars. All that was achieved, however (as reported by the National Cancer Institute at the beginning of 1967), was that the progress made in the field of the chemotherapy of cancer makes it possible to look to the future with hope. Success was achieved in producing an exceptionally long-term remission in children suffering from the acute form of leukosis (over 100 children are still living five and more years after treatment), and a group of females who had suffered from chorionepithelioma have survived for five or more years.

Just as in the rest of the world, medical specialists in the Soviet Union are exploring for rational ways of discovering anti-tumoral drugs in conformity with the chemical structure of the substance, its biological activity and so forth. Even so, no less than a thousand preparations are examined by specialists every year. According to information released by the Board of Oncological Aid under the USSR Ministry of Public Health, 2200 synthetic compounds, plant-derived preparations and antibiotics were tested in 1976. Among them, only two per cent proved to possess the required properties. Moreover, according to the world experience, only a negligible part of the substances which can inhibit the growth of cancerous cells in animals has proved to be applicable in clinical practice.

Chemotherapy, unfortunately, has yet to accomplish the expected revolution in oncology, but with the aid of drugs, it is quite possible to cure most patients suffering from up to six different forms of malignant tumours without resorting to operations and radiation therapy. This primarily concerns acute lympholeukosis in children, Burkitt's lymphoma, chorionepithelioma of the uterus. In approximately another 16 forms of cancer, therapeutic agents supplement non-radical methods and may extend the life and alleviate the suffering of patients for whom surgery or radiation therapy is contraindicated for a variety of reasons. With the development of new anti-tumoral agents, however, and the refinement of regimes for the effective application of known agents, the possibilities of chemotherapy in certain diseases are substantially different.

Just as in everything that concerns oncology, the results of chemotherapy decisively depend on the competence of the physician. In medical practice today doctors rarely restrict treatment to only one or another agent. It is theoretically sound to simultaneously apply various methods which, first of all, disturb the metabolism of tumour cells at different levels, and second, which strike down tumour cells at various stages of their division. It is most important to avoid identical side effects so as not to intensify the toxicity. The most successful combinations of chemical agents, as a rule, are far more effective than any single one of them separately.

Drug therapy of cancer cannot be confined to narrow specific limits; it is aided by hormones and substances controlling the body's own defense forces. The hormonal treatment of cancer is a very complex field. The reader no doubt remembers that it is not only based on concepts of the hormonal dependence of some forms of malignant tumours, but also on the significance of hormones in the ageing of the organism and other biological transformations.

The birth of this method is linked with the name of the American Charles Huggins. After many laborious complicated experiments he defined the role of antagonists of a male sex hormone in the counteraction to carcinoma of the prostate. He was awarded the Nobel prize in 1966 for his outstanding discovery, but the value of this discovery proved to be more extensive because he formulated two new principles of oncology which formed the basis of hormone therapy: (1) cancer is not necessarily an autonomous and internally self-supporting process; (2) hormonal secretion may not hinder but may even stimulate the development of cancer in ordinary, heightened or reduced levels of activity.

A special effect, as might have been expected, is achieved in treatment of hormone-dependent tumours such as carcinoma of the uterus, the thyroid, prostate and mammary glands.

It has long been known that the development of breast cancer is influenced by sex hormones and in many cases of advanced disease, the ovaries are removed. This measure, however, is not always sufficient: the spread of metastases does not stop, most likely because hormones continue to be produced by the adrenal glands "assuming" part of the lost functions of the ovaries. Ever since artificial adrenal hormones essential for life were synthesized in the fifties, it became possible to live without this organ. Patients, however, react to this operation as to a severe trauma and for the rest of their life are "dependent on the drugstore".

Based on the fact that hepatic cells can destroy sex hormones without harming others secreted by the adrenals, the late Professor N.N. Alexandrov and his pupils developed an operation for the purpose of ensuring the outflow of blood from one of the adrenals exclusively through the liver. The first transplants of the patient's own adrenal produced promising results: the lives of a group of female patients suffering from a very advanced stage of breast cancer were prolonged by 37 months on the average, i.e., by more than three years. What does a "gift" of three extra years of life mean in our times? Science is consistently working to vary the arsenal of ways and means, and who knows what doctors will be able to do within the near future?.. The following is a concrete example:

A middle-aged woman came to the P.A. Herzen Institute for consultation. Always busy with interesting work, obligations as a mother and wife, she had not paid attention to her health and had neglected the changes that had occurred in her breast, the enlargement of lymph nodes. Examination revealed a thriving breast cancer with multiple metastases in the bones.

A group of doctors approved an optimal plan of treatment for her. Despite the extensive spread of the disease it was decided to begin with an operation to remove her breast, to reduce the volume of tumoral tissue in the organism, and to improve conditions for drug therapy. The ovaries were simultaneously resected, which allowed for the effective use of hormones. Immediately after the operation infusion of anti-tumoral chemical and hormonal agents was begun. While the inevitably sad end was delayed from month to month, an extremely active synthetic anti-hormonal preparation was found and was expected to have a decisive effect.

Without going into the medical details, about seven years have elapsed since then. The former patient is now head of a department, travels on business trips and is raising her grandchild. There is no doubt that had she fallen ill in 1970 and not in 1977 this woman would have died. All of this does not mean that we can now save any patient suffering from breast cancer no matter at what stage it may be. There are still forms which we, unfortunately, are powerless to cure.

Huggins's concept that cancer is not necessarily autonomous along with the data of Silber and his followers on the presence of immune shifts in the organism identifiable by laboratory tests, gave rise to the development of a new science—clinical immunology. The reader has already been acquainted with this field. Although the first experiments are still not very convincing, research in this direction is being accelerated.

Scientists investigating conservative methods of cancer treatment are now staking great hopes on interferon. Produced in response to a viral infection, it inhibits replication of the virus and serves as the organism's first line of defense. The idea of using interferon for treating tumours was conceived due to its ability in tissue culture to suppress the growth of tumour cells more effectively than of normal cells, as well as on the premise that many tumours are evidently caused by oncogenic viruses.

There have already been reports in the literature about successful trials with interferon. One should not forget, however (and this is underscored even by advocates of the agent) that testing of interferon has just begun.

As was stated, prior to 1900, oncologists had not registered any cases of a stable cure from malignant tumours. By 1937, approximately 25 per cent of patients were cured by radical methods and by the beginning of the eighties, already more than 40 per cent.

All efforts by administrators of public health care, doctors and their assistants involved in early diagnostics, oncologic surgeons, specialists in chemo- and radiation therapy. endocrinologists and immunologists bear fruit. As a reminder—in the Soviet Union there are approximately a million people who have been cured of cancer and half of them survived for more than ten years.

The older generation of physicians still remembers the time when all they could do was calm the fears of the cancer patients, or at least delay death for a short time.

Today, patients who had until recently been considered doomed are being saved from such a tragic end. The basic tendency of progress in oncology is very promising and the authors of this book share the opinion of the Nobel prize winner Peter Medawar who is confident that the events that are considered heroic today will become part of standard medical practice tomorrow.

As a science, oncology began with the registration of patients and, for quite a while, those who were afflicted with cancer equalled in number those who died. The only source of information about the spread of malignant tumours boiled down to mortality statistics. Nowadays, however, mortality from this disease has been greatly reduced. This gives us the right to state that we are witnessing the genesis of cancer survival statistics.

The Doctor and the Patient

Speaking of his profession, the Honoured Test-Pilot of the USSR Mark Gallai wrote: "One cannot take a single step forward in our field without coming up against still another moral and ethical problem!" He spoke of a sphere of human activity where the links are between man and machine. In medicine, where the contact between man and man is direct, it is quite natural that the number of moral and ethical problems and the degree of their acuteness increase immeasurably.

Since ancient times some physicians, statesmen, philosophers and writers have attempted to define these interrelations and place them in a certain framework.

The importance of a doctor's mission distinguishes him from people in other specialities. There is probably no other field of human endeavour that is bound by such a vast number of exhortations, rules, obligations and even pledges that developed around medicine in the long centuries of its existence.

The humane ideas expressed in the works of Hippocrates most influenced the formation of the image of a physician and his relations with the patient. One of these ideas in effect stated that the physician-philosopher may be likened to God because there are few differences between wisdom and medicine, and all that one searches for to obtain wisdom is known to medicine, namely, contempt for money, conscientiousness, modesty, simplicity in dress, respect, judgement, decisiveness, tidiness, an abundance of ideas, knowledge of everything that is essential for life, etc.

Despite the fact that these ideas were expressed 25 centuries ago, much that Hippocrates taught sounds very contemporary: Whatever home I may enter, I go to benefit the patient, for I am far removed from any bad intent, anything that is unjust or baneful. Whatever I might see or hear about human life that should not be divulged, I shall not speak about, considering such things to be secret...

When one reads Hippocrates one begins to realize that a good physician in ancient times was hardly different in his thinking and behaviour from a good doctor practising in our time. The contemporary doctor simply has more possibilities for diagnosing and curing diseases. The concept of "the doctor's ethics" in the past, however, included the doctor's personality, his interests and status in society. In a society based on the principle of buy-and-sell, doctors naturally turned into entrepreneurs acquiring capital on fees paid by patients. In *Medical Guide*, a handbook published in the tenth century, the following advice is offered: ...Visit your patient when he is feeling very sick. Make sure to reach an agreement on your fee at this moment, because as soon as he is feeling better, he will forget everything.

The greed of some "healers" made physicians targets of mockery and jeering. Even Sylvius, the great anatomist and physician of the Renaissance, who is known in the history of medicine for his faults as much as for his merits, became the subject of the ultimate gibe. On the day of his death an ironic note was pinned to the doors of the church where the funeral was held: "Here lies Silvius, who did nothing free of charge; he died for free, which is sad to discover."

The mercantile aspect of medicine is very evident today in the capitalist countries. F. Dickinson, one of the directors of the American Medical Association, frankly stated that the doctor is interested in business, just like anybody else selling his wares. The social commentator and author F.J. Cook even titled his book about health care in the United States *The Plot Against the Patient.*

As surgeons of quite another formation, the authors of this book were dismayed to learn from the memoirs of the outstanding French surgeon Rene Leriche that ... the surgeon earns his living by surgery. One has to live. The physician feels so much better when he is free to make such a royal gift as health, working selflessly, without having to think about being paid for such a present...

As any bargain drawn up by the sides, the rights and responsibilities of physician and patient have been specified by law since time immemorial. In many ancient states, for example, the physician had to pay a fine if he had unsuccessfully treated his patient, while in ancient Babylon he could even have been executed.

As a rule, however, the question of responsibility was never brought up, particularly when it was common people who were unsuccessfully treated. This was wickedly underscored by the playwright Moliere in his *Le Malade Imaginaire* who made the doctor in the play recite the following cynical monologue:

"The position of a doctor attending the great in the world never attracted me. I was always of the opinion that it was far better for us sinners to keep to the simple folk. It is much easier: you are responsible to nobody for your actions, you just have to keep to the rules of science without worrying what it will come to. With the great of the world this becomes a great bother because when they fall ill their resolute desire is to be cured by the doctor without fail..."

This, of course, was presented by Moliere in grotesque style. Reality sometimes seriously departed from the norm. It is said that when King Charles IX told his court physician Ambroise Paré that he should be cared for better than the common folk the doctor boldly replied that he treated the poor just as carefully as kings.

The qualifications of a doctor do not only include his knowledge and professional experience, but also the intimate qualities of his heart and soul. A poll conducted by Polish sociologists several years ago revealed what significance patients attach to the purely humane traits of their doctor: only 39.5 per cent of those canvassed wished to be treated by a famous physician, whereas 60.3 per cent of the 3200 people who took part in the poll wanted a doctor who did not enjoy as much fame but was known for his sincerity and concern for the patient.

It would seem that any person employed in the human services professions is obligated to follow the recognized rules of behaviour, but in medicine the proper behaviour is not determined by rationale, nor by the considerations of politeness, but by the humaneness of the medical profession itself. Actually the sole purpose to which a person with medical training devotes himself is to render aid, whether by studying the causes of a disease, its prophylaxis, surgery, or the organization of public health care. The fact that the training of medical cadres is now conducted on a mass scale can be evaluated in two ways: Without a giant army of medical specialists it would be impossible to reach the population of such a large country as the USSR; therefore, this is an objective necessity. On the other hand, the ability to choose one's profession is practically out of the question and there is a greater element of chance involved in choosing one's life work.

It rarely happens now that a young man becomes a doctor because of an insurmountable desire to do so as happened with the outstanding Soviet surgeon N.I. Pirogov or with the German physician Albert Schweitzer. The latter's story is quite remarkable: At thirty years of age, when Schweitzer was a professor of philosophy and theology at Strasbourg University and an organ musician well-known in Europe, he made up his mind to become a doctor and entered the medical faculty of the same educational institution where he worked as a professor. The overwhelming majority of physicians realize that their true calling is medicine later in life.

It would obviously not be correct to speak of anyone having an inborn inclination for medicine, just as some do for music or mathematics. One can only speak of the development of certain properties of the intellect in the process of receiving education and training. The moral requirements are easier to formulate: people who are indifferent, callous, egotistic or simply cruel should never be allowed to become physicians.

Foreseeing the broader invasion of medicine by technology and automation Antoine de Saint-Exupery once remarked with sad irony that he believed the day will come when a person stricken by an unknown disease will put himself at a mercy of physicists. Without questioning him about anything they will take a blood test, figure out some constants, multiply them and then, using a slide rule, they will cure him with a single pill. Nevertheless, he continued, he himself preferred going to some old country doctor who would look at him from the corner of his eye, take his pulse, palpate his stomach and examine him with a stethoscope. This doctor would then cough, light his pipe, rub his chin in meditation and smile to alleviate whatever pain he might feel. "Naturally, I admire science," concluded Saint-Exupery, "but I admire wisdom no less."

A good doctor does not heal with drugs alone, but with the power of a kind word. This is inherent in the very essence of the healer's profession. The word "vrach" (in Russian) derives from the ancient Russian verb "vrat" "to lie", i.e., to calm and soothe the patient's apprehensions with a "white lie".

The formation of the moral and ethical principles of healing takes place not so much based on instructions and pledges as under the influence of the living example of specialists of the older generation.

There is a concept in medicine known as "the physician's secret". Usually this implies the obligation of the attending physician not to make known to others the intimate details of the life and health of his patient. This actually is the secret of the patient. The true physician's secret is the secret of the art of medicine. This secret is amassed particle by particle and, thus, to use the apt expression of K.G. Paustovsky, "the golden rose" of clinical experience is formed.

There is an age-old maxim to the effect that the teacher must teach and bring up his pupil. Within the framework of the subject in hand this means that the teacher must teach his pupil the subtleties of the medical profession, but most importantly, he must teach his pupil to love people selflessly, to relate to his patient as to a brother or sister, to bow only to the truth and to make all his actions respond to the finer traits of his heart and soul.

In Russian medicine one finds many examples of the best kind. One is involuntarily reminded of the "great philanthropist" F.P. Haaz, who was a prison doctor in the first half of the 19th century, and whose motto in life was, "Make haste to do good!". Nikolai Pirogov is an excellent example of a physician who was openly critical of his own mistakes in medical practice. He boldly discussed his errors in the press and stated that every doctor can make a mistake but has no right to conceal it. Somewhat later, another famous surgeon, the Austrian Theodore Billroth, who played a part in the fate of Dr. Pirogov (see the end of the chapter), wrote that only people who are weak in spirit, boastful, and world-weary fear to come out into the open about the mistakes they have made. Those who feel strong enough to do better experience no fear in admitting that they had erred in something.

One must remember the cohort of country doctors headed by E.A. Osipov who brought their love and loyalty to the common people and comforted them in their suffering by word and deed.

It is obvious that if one had never read the stories of Dr. A.P. Chekhov and Dr. V.V. Veresayev, literature would not only have lost some of its richness, but the living representatives of the medical profession would be lacking some very important character traits. The following are the fine and lofty words stated by one of Chekhov's characters who made up his mind to become a physician: "The profession of a doctor is an exploit which calls for self-assertion, a purity of spirit and clarity of intention. One must be of bright intelligence, pure in morals and physically tidy."

Among unforgettable Russian teachers are the contemporaries S.S. Yudin, Academician and surgeon, and I.A. Kassirsky, Academician and general practitioner, but a particularly prominent role belongs to N.N. Petrov. It is not by chance that one of the most outstanding oncologists in the USSR founded the field of study about the principles of behaviour of medical personnel (medical deontology).

Oncology is a very special field of medicine where the highly specialized training of the physician must equal his ability to make contact with his patients. A violation of this unity may grievously effect the fate of the patient.

The main problem lies in the fact that any kind of slips or errors made by the oncologist are not evident immediately as in acute diseases requiring surgical or general treatment. They come to light only after some time, even after a long period of time when it becomes very hard, if not entirely impossible, to eliminate the mistake. Moreover, the biological property of tumours to continue growing and the general lack of faith that people have in a stable cure for cancer may, to some extent, disguise the medical error or sometimes, to put it crudely, allow one "to write it off". That is another reason why the oncologist must live with a constant feeling of high moral responsibility for the fate of every patient he encounters in his practice.

On the other hand, the oncologist has to deal with people who have been psychologically traumatized by the conviction that they are afflicted with an incurable disease or that they must undergo surgery. The ability to win the absolute confidence of the patient is an indispensable component of successful treatment.

Nikolai Petrov himself is a model of both a doctor and a human being, and his small book concerning problems in deontology is written with heartfelt sincerity. Today, more than 30 years after it was published, it is acknowledged as a canon for the younger generation written by an eminent clinicist and scientist of immense wisdom and experience.

"Deontological considerations must be present at all times in surgical work; they must permeate all stages of surgery just as letters, spelling and grammar are omnipresent in literary work. It becomes particularly clear as to how important it is for surgeons to become complete healers; that is, they should accept the burden of concerning themselves with curing not only the patient's body, but also his soul, and they should devote not only all their knowledge and skill to the patient, but also their best feelings and the kindest attention."

Much of what Petrov said is so aphoristic that it has become part of the golden fund of medical proverbs and sayings:

"Surgery is for patients and not for surgery.

"Boldness should never exceed skill.

"The patient would prefer to be alive after a palliative operation than dead after a radical one.

"The patient is always a human personality with all his complexity of emotions and not just another medical case." And the list continues.

Deontological problems also concerned another founding father of Russian oncology, namely, P.A. Herzen, in whose articles and reports one finds interesting ideas regarding this aspect of medicine. For example, in analyzing the reasons for late diagnosis of breast cancer, P.A. Herzen wrote: "A woman neglects seeing a doctor for a variety of reasons: she may feel bashful or she may have a careless attitude to her own health, but the main barrier is that she fears the doctor might reveal that she has cancer. This peculiar behaviour is very common and plain observation shows the importance of, on the one hand, medically enlightening the female population and, on the other, how cautiously, even *tenderly* (underlined by the authors), one must approach the psychologically distressed woman who had already noticed an unusual hardness in her breast which does not resolve."

Although this book is written for a wide circle of readers, the authors could not ignore questions of deontology for the following reasons: first of all, the medical profession in the Soviet Union today is developing on a mass scale and this book may easily reach the hands of a young physician, doctor's assistant or nurse; and second, every reader must know what type of behaviour is required of a person wearing a white smock

Before all else, it must again be emphasized that the doctor is a public figure. He toils constantly for people and among people and there can be nothing more humane than his mission in life. The high requirements placed on a doctor in the Soviet Union are stated generally and solemnly in the "Pledge of a Physician in the Soviet Union" established by Decree of the Presidium of the USSR Supreme Soviet in March 1971.

"On receiving the elevated title of Physician," reads the Pledge, "and beginning to work as a doctor, I solemnly swear:

"to devote all my knowledge and strength to protecting and improving the health of Man, to the treatment and prevention of diseases, to work honestly wherever the interests of society call for my effort;

"to be always ready to render medical aid, to show attention and care for my patient, to keep the physician's secret;

"to constantly improve my medical knowledge and doctor's skill, to promote by my labour the development of medical science and practice;

"to turn for advice, if the interests of the patient call for this, to my professional colleagues and never to refuse them help or advice should they apply to me;

"to treasure and develop the noble traditions of my country's medicine, in all my actions to be guided by the principle of communist morals and to never forget the high calling of a Soviet physician, his responsibility to the people and the Soviet state."

Irresponsible action often causes substantial harm to the reputation of a medical establishment which at times cannot be undone. Bad manners, rudeness on the part of the nurses and medical personnel may traumatize a patient who is not well as it is.

The following are a few frank admissions made by one of the author's patients just before leaving the hospital. It is fortunate that, despite the serious operation he had undergone, his natural sense of humour remained:

"On the very first day of my admission to the hospital a quick test of my sense organs was given. As I entered the ward somebody hollered:

"'Where do you think you are going? Are you blind?!'

"This nurse was interested in my eyesight.

"'Or are you deaf too?!'

"My hearing was also being checked.

"At another time a nurse came rushing into the ward screaming, 'Hurry up, stop messing around there!'

"That scared me. I placed a validol tablet under my tongue. Where were they taking me?

"It turned out that I was being led to a neurologist to calm my nerves."

The role of nurses in creating a favourable atmosphere cannot be overestimated. Many of them fully understand why they are needed in the oncological service and correctly judge the nervous state of the patients. The work and duties of an oncological nurse are very complicated and far from every young girl is inherently capable of comprehending the specifics of this branch of medicine.

In his book on deontology, S.B. Korzh cites the following example:

"Nurse X. fullfilled her medical duties correctly and accurately and was never officially reprimanded for her work, but the facts show that her choice of profession had been unfortunate and that she lacked the qualities that medical personnel must have.

"Once a patient requested a pill because she had a headache. After an hour had passed and no pill had been brought, the patient reminded the nurse of her request. This angered the nurse, who responded by saying: "The headache won't kill you; you'll die from the disease you came here with." All the other patients in the ward who were being treated for carcinoma of the cervix heard this remark. They became extremely upset and there was no end to tears. A month later the same nurse replied to another patient who had asked her what diagnosis the doctors had established: "If I tell you the doctor will cut out my tongue."

"Such callousness made the doctor in charge summon the nurse to his office for explanation, but her reaction was summed up in her response, "I can't make the sun shine for them."

The reader can now see that the profession of an oncologist is among the most difficult in medicine. The physician who chooses this speciality must accumulate a vast amount of knowledge in biology, surgery, radiation therapy, chemotherapy and immunology. Without such reserves of knowledge he will find it extremely difficult to select and implement the most optimal plan for treating the great variety of cancer patients that seek his help. The most complicated problem he will have to tackle, however, is purely psychological, because he will be in daily contact with victims of cancer, who are overwhelmed by fear and doubts, and with their relatives, who are often on the verge of despair but are obliged to remain calm and optimistic in the presence of the patient. The oncologist bears the brunt of all these emotions, and not only the moods, but also the fates of many people depend on his emotional state. Korzh told about a nurse who did not wish "to make the sun shine for her patients", but the oncologist absolutely must make the sun shine for his patients, otherwise he will not truly help them. This may strain him to the limit, but it is necessary.

Some doctors, who do not consciously control their behaviour, work "by intuition" without relying on the clear-cut rules of deontology outlined by Petrov, and they go to either one of two extremes. Some of them begin to pity every patient whom they cannot radically cure; they become worried and lose their composure, which generally influences the results of their activities. Others develop complete indifference to their patients, calmly reacting to lethal outcomes of operations they have performed and, during discussions of important questions at hand, they juggle with statistics forgetting that for the patient his health is of 100-per-cent concern. Such doctors very quickly cease to bring "sunshine" to the people who entrusted them with their health.

It is none other than these groups of doctors, described above, that tend to make bad mistakes in deontology. It is a banal truth that all people are different, with different backgrounds, tastes and views. The doctor, however, who has chosen oncology, with its responsibilities, as his profession, must find strength and reasoning power to constantly analyze his own slips and errors and consciously try not to repeat them. One person may be hasty by nature, another may be quietly assured, but both must watch their steps because deontological mistakes most often result not so much from negligence as from flaws in the physician's character. The people who most often make mistakes are those who are quick to take offense, garrulous, hasty in making judgements and forming opinions, inclined to exaggeration of their knowledge and, at times, of their official status.

If a doctor can be critical of himself he can, knowing his faults, carefully control his actions. If the doctor thinks it unnecessary to change his ways and manner, and stubbornly keeps on making deontological mistakes, it is the duty of his elder colleagues to tell him that he is not professionally fit for oncology. This is also an operation of sorts that, although it is painful, must be carried out.

An oncologist must always be calm, attentive, knowledgeable and kind. He must respond not only to the physical, but also the mental, state of his patient, because psychological changes are practically an ever-present component of an oncological disease. The doctor must perform his duties despite his own bad moods, emotions, sympathies and antipathies. Petrov's well-known maxim stands firm: "Surgery reaches the peaks of its possibilities only if it is attended by the highest manifestations of unselfish concern for the patient and not only for his body, but for his mental state, his psychological condition."

It must be emphasized that the gigantic progress of surgery is to a great measure due to the development of humane methods of treatment (anaesthesia, organ-preserving operations instead of amputations, and so on) in the endeavour to spare the patient new sources of pain and suffering.

Although it is not original, in order to give an idea of what the work of a surgeon is like, to compare his profession with others. A malignant tumour is like a shrapnel time-bomb which, unless quickly rendered harmless, will explode (metastasize) and kill the patient. The oncological surgeon may thus be likened to a combat engineer in battle, and like the combat engineer, he has no right to make a mistake. True, there is a difference: the surgeon's mistake spells death for the patient, but not for himself. The oncologist's profession is also similar to that of a test-pilot, because in both, one has to make split-second decisions during complicated tasks in unexpected circumstances.

As distinct from biological scientists whose investigations of cancer are conducted on a global scale, the surgeon fights for the life of just one person each time; however they add up and tens and hundreds of lives are saved from the clutches of death.

The ancient commandment of medicine "to do no harm" is just as vital today, but one must bear in mind that caution is not the same as passivity. Now that the possibilities of surgery have multiplied immeasurably, the oncological surgeon is confronted not only with medical, but also with philosophical issues. Has he any right to perform crippling surgery? Is it just to cause infinite suffering? It is very hard to answer such questions! If the alternative to an operation, however, is slow, torturous death, the doctor's duty lies in preserving life and making it at least tolerable.

One can easily understand the surgeon in Christiaan Barnard's novel who perceives death as an enemy, to whom yielding without a struggle means committing the worst of treacheries. Other aphorisms could illustrate the point, but these words were chosen because they were the thought of the man who performed the first heart transplant in history.

In order to save a life, the oncologist is sometimes forced to take a risk, and lethal outcomes are bound to occur Lethality is derived from the Latin word "letum", which means "death". Lethe, a river in Hades whose waters cause drinkers to forget their past, is closely related to lethality. There are various ways and methods of treating diseases that make it possible to reduce the mortality rate, and medicine is mainly engaged in this, and quite successfully, at that. But the ways of reducing mortality are not only with new medical agents, antibiotics and surgical methods. These ways are literally the paths that link the home of the surgeon with the hospital; they include personal contact with the patient, the ability of the physician to share the concerns of the patient and to instill confidence in the patient that he will recover.

In the detective story *A Visit to the Minotaur* by the Weiner brothers, the famous violin craftsman Amati tells his pupil Antonio Stradivari:

"I never work when I am in a bad mood, so that no accidental cut may be made that has not been carefully figured out, even felt..."

This statement came to mind because there are times in the life of a surgeon, unfortunately, when he is obliged to perform an operation while rundown, offended or upset. And it is not wood but living tissue that he has to cut...

Deontology also deals with relations among medical colleagues. A great many ungrounded complaints by patients about allegedly incorrect treatment are caused unintentionally or purposely by the desire of some doctor to win prestige with his patients by making derogatory remarks about his colleagues. Under ordinary circumstances this is just regarded as a cheap trick, but in a hospital it is the patients who suffer, and at times pay a heavy price. The following case is an example of this:

A young teacher once noticed that a growth had appeared in her breast. Within days she was hospitalized in an oncological ward where the doctors found that the process was far advanced due to neglect and radical treatment was out of the question. A plan for drug and radiation therapy was duly elaborated and the woman was told a mild version of her disease, which she believed. Fortunately, the tumour proved highly sensitive to treatment, which was repeated from time to time over a period of four years. The patient felt better and even well enough to work. This state of affairs might have continued indefinitely but she met a doctor who declared that she had been treated incorrectly and that an urgent operation was necessary before metastases set in. Medical specialists tried hard to persuade the poor woman that her former treatment was quite effective for the time being, but her confidence had been shattered. She wilted visibly, her resistance to the disease diminished, the process generalized anew and the patient died.

Unfortunately, there are many such examples. It is no wonder that an ancient healer's prayer reads: "Make my patients trust me and my art, chase away all the quacks from the patient's bedside..." The problem is much more serious and complicated when the matter concerns professionally educated medical specialists, some of whom may be very famous.

It is quite understandable that the cancer patient and his relatives wish to make sure that nothing is left to chance. To avoid offending the attendant physician, such verifications are often done in secret, although it would be more expedient to include him in the consultation, or to at least let him know politely that one is exploring other possibilities. The experience of the authors shows that an intelligent physician never becomes offended by such action. This is in fact absolutely necessary because the "secret" consultant simply does not have all the first-hand information about the patient and may reach an erroneous conclusion.

When resorting to expertise, the interested persons should also know that there are different trends and schools in oncology. In breast cancer, for instance, the Leningrad school of oncology has for many years advocated and regularly practised post-operative chemotherapy, even in comparatively early stages of the disease. At the same time, only surgical treatment was employed at the P.A. Herzen Oncological Institute in Moscow for these stages of the disease. Analysis of the remote results of both approaches produced practically identical data; therefore they may be considered equally applicable until large-scale research now being carried out in many countries is completed in order to objectively establish which is the optimal method.

Only after evaluating the prescribed treatment or the treatment that has already been carried out, can the consultant then cautiously suggest the corrections he has in mind if he is sure of the insufficiency or inadequacy of the measures that have been taken based not just on his personal point of view, but on the fundamental factors of the prognosis. For example, in oncology today, irrespective of the directives adhered to in a specific clinic, it is considered a "must" to include supplementary methods in the plan for treating breast cancer with metastasis into the lymph nodes. At the current stage of development in oncology, this is generally accepted and the question is only in choosing among radiation therapy, chemotherapy, etc., as well as the proper sequence of their application. Therefore, if the consultant sees that the attending physician has stopped halfway, and limited his treatment to surgical intervention, he must correct the physician, but delicately, such that the patient does not get the idea that she has been treated incorrectly. If chemotherapy was the chosen treatment, while the consultant prefers a combination of radiation and hormonal therapy, he has no moral right to change what has been prescribed.

It is only in exchanges with the attending physician and, by no means, with the patient that one may state his reasons and grounds for changing treatment approaches. Any other behaviour on the part of the consultant is likely to perturb the patient and raise his or her doubts leading to all the consequences.

Deontology deals with many questions. One vital problem is, What should the oncological patient know about the disease he is suffering from? This question (as a specific case of Truth and Lies in relations between people) was most acutely posed by Lev Tolstoi in his story *The Death of Ivan Ilyich.*

"Only one question remained prominent in Ivan Ilyich's mind: Was his condition dangerous or not? The doctor ignored this awkward question. From the doctor's viewpoint this was a useless question not worth discussing. It was only necessary to weigh the probabilities: a wandering kidney, chronic catarrh or a diseased caecum. It was not a question of the life or death of Ivan Ilyich, but an argument between a wandering kidney and the caecum. And Ivan Ilyich saw this argument brilliantly resolved by the doctor in favour of the caecum with the stipulation that a urine test would provide new evidence and then the matter would have to be reviewed."

It is not surprising that after talking to the doctor, purely professional judicial associations entered the thoughts of Ivan Ilyich, namely, "everything was exactly what Ivan Ilyich himself had done a thousand times, in such a brilliant manner, with defendents in court. The doctor summed up his conclusions just as brilliantly and looked at the defendent over the top of his spectacles merrily, even triumphantly. Ivan Ilyich understood that he was in a poor condition, while the doctor and probably everybody else simply did not care. This conclusion caused Ivan Ilyich much pain, evoking him to feel pity for himself and spite for the indifferent physician who showed no concern for such a vital question as his health. He got up without a word, put the fee on the table, sighed and said: 'We patients obviously very often ask useless questions. Generally speaking, is mine a dangerous disease or not?'

"The doctor looked sternly at him with one eye as if to say: 'Defendent, unless you refrain from irrelevant questions, I shall be obliged to order you to leave the courtroom.'

'I have already stated what I considered relevant and convenient. Investigation will show what else might be pertinent.' With that, the doctor bowed politely.

"All the way home Ivan Ilyich kept remembering everything the doctor had said. trying to get at the meaning of all those confusing scientific terms, hoping to translate them into simple language and find a reply to his question, whether his condition was poor, very poor or not too bad as yet. It seemed to him that his condition was very bad... The aching pain did not cease for a second and because of the confusing words of the physician this pain seemed to have acquired another, more serious significance."

If one looks at this excerpt from a professional point of view it is easy to see that it is an excellent illustration of how relations between doctor and patient should NOT be built. Although the doctor said nothing at all about the dangerous disease, Ivan Ilyich realized that his chances of recovery were very slim. This became obvious to him because the cold indifference of the physician was evident in his manner and every single phrase that was uttered. It is common knowledge that the tone of voice creates the whole atmosphere, not only the words are important, but the meaning they conceal. Within the limits of professional medical behaviour, the physician could have given the sick man spiritual support through compassion and sympathy.

The sincerity of the doctor calls for deep wisdom, thoughtful tact and heartfelt warmth. The slightest deviation from this will give rise to falsity or cynicism.

Nevertheless, is the oncologist obliged to be honest with his patients completely? Everybody knows that a person's mentality and behaviour changes from the moment he learns that he is seriously ill, that he is about to be operated on, or that he will have enter the hospital for a long stay. The word "cancer" strikes like an explosive shell of the heaviest calibre.

In *The Sentence* V. Soloukhin very sincerely and graphically describes the mental state of his lyrical hero after he has visited the oncologist: "Suddenly, with clear-cut merciless clarity I realized, while walking from the doctor's office to the cloakroom, that my life before my visit to the doctor and my life after I had been examined were already two different existences with different laws, different passages of time, different understanding of what is important and what is unimportant, just as the life of a country can be before and after war is declared..."

The psychology of a sick person resembles the psychology of a "naked man", i.e., somebody who is unprotected and very vulnerable as he stands before the physician. This produces the extreme hypertrophy of the "white smock", the appearance of which in the patient's ward invariably gives rise to a wave of concern, hope and fear.

The oncologist has to take into account

the sharpened feeling of doom inherent in his patients. And if the patient is openly informed of the diagnosis, even in the event of favourable treatment results, he will experience the same emotions as the hero of the story *The Lord's Spear* by Bunin:

"...this yellow flag of death under which we now float—it is the yellow hospital pennant which keeps reminding you to always be ready for death, which is over you, in front of you and all around you..."

Hippocrates in his time understood this profoundly. He preached: "Surround the patient with loving care and consolation, but the main thing is to leave him unaware of what is in store for him, particularly what threatens him."

One could agree with this if not for a number of circumstances. To begin with, there are never any standard reactions and the acuity of perceptions widely ranges in different people. It can be said that every human lives, falls ill and either recovers or dies in his own way; therefore, the question whether or not to tell the patient what he should expect cannot be given a proper reply.

Gregor Mendel, who established the laws of heredity, demanded a clear answer about his condition from his physicians when he fell seriously ill. When they told him that he was fatally ill, he remarked, "a natural inevitability".

When the famous Russian surgeon V.A. Oppel fell ill with a malignant tumour of the maxillary sinus he trained himself to see with just one eye, because he knew that after an operation the loss of vision in one eye was inevitable, and he wished to continue his work as a surgeon.

Georges Pompidou, the former President of France, who died in 1974 from a malignant disease of the blood, was a courageous man. He knew that the disease was incurable but stayed at his post to the last.

There have been many examples of such courage. The ability to penetrate the psychology of the patient is a task with many unknown factors. Unfortunately, it is not every physician that is equal to this task.

Since the investigations conducted by Ivan Pavlov it has been known that the reaction of the patient to deterioration in his health and forthcoming treatment depends to a large degree on the type of his nervous activity. "Sanguine" types behave most courageously and the sign "oncological" on the front of a medical centre or an institute does not, as a rule, cause them to fear or panic. In unforeseen complications they do not loose spirit and even try to cheer up their doctor if they notice that he is alarmed or nervous.

Norman Cousins, the American writer and scholar who recently wrote the book *Anatomy of an Illness* was obviously this type of person because he succeeded in overcoming a severe illness by means of a simple method which he dubbed "laugh therapy". The theoretical premises for his method could be described as follows: if negative emotions, according to the Selye theory, induce stress and have a negative influence on the organism, then positive emotions (joy, love, faith and laughter) should have an opposite effect.

Cousins came to the conclusion that the will to live is not an abstract concept, but "a physiological factor of therapeutic significance". Therefore, when "the tandem", composed of doctor and patient, undertakes everything possible to activate the reserves of the organism and the will to live, this will yield positive results.

The habit of conversing with the patient is developing with years of insistent work. The experience of the authors indicate that in serious cases, prior to a complex hazardous operation or intensive radiation or drug therapy, or when a loss in working capacity is expected after being cured of cancer, the talk with the patient or his relatives is usually conducted by the most experienced doctor who commands the greatest respect, or sometimes, by two or three doctors.

In the doctor-patient-relatives relationship dissension occurs for a variety of reasons. Most often the patient, feeling that the doctor has not given him complete information, seeks it elsewhere, listening to the idle talk of others in the ward, of the less-specialized medical personnel, and reaches his own, very often erroneous, conclusions. The difference in data collected from various sources arouses distrust and doubts which only make things worse.

Volumes have been written on how the doctor and other medical personnel should behave, but unfortunately practically nothing has been written about the proper attitude of the patient to the doctor and his helpers. Too much insistence and reiteration of questions that have already been answered, accompanied by nervousness and sharpness of tone, to say nothing of ungrounded complaints about the physician, not only hurt him, but often deprive him of peace and sleep. It must be remembered that the Soviet public health system maintains strict control over the activities of medical institutions and their staffs.

The most effective, not always pleasant, but stern, control is accomplished by the doctor's colleagues. These opinions are aired every day at morning staff conferences where patients who will undergo surgery are discussed. At such discussions all the doctors involved have the right to voice their opinions: the young oncologist who just performed his first operation and the grey-haired veteran must equally prove their professionalism, explaining how what they plan to undertake is the best treatment indicated for each individual patient. The next morning they must honestly report on the results of what they did and whether or not they adhered to the advice offered by their peers on the preceding day. If the patient dies, the circumstances of his death are discussed and analyzed as soon as possible. Any excuses, such as sleepless nights, agonizing doubts, or successes that had been scored earlier in similar cases are not taken into consideration. The only focus of interest is whether everything was done and what still could have been done to help the patient to recover.

The work of an oncological surgeon calls for maximum exertion, mobilization of thoughts, and time. Every death of a patient, no matter how many years the physician had been practising in oncology, means heavy suffering for the doctor, affecting his health, feelings and even his family life. For years on end the oncological surgeon cannot go to the theatre or visit his friends without notifying the doctor on duty of his whereabouts. All his life, meetings with others, conversations and amusements seem to be unconnected intermissions between the acts of a long tragic play entitled *Surgery*. The average duration of the working capacity and even life of surgeons is much shorter than of people in other occupations, even if there are proven occupational hazards to their health.

The history of medicine knows of tragic cases when the surgeon was so shocked by the death of his patient that he committed suicide. In 1928 there were two simultaneous funerals in Saratov following the deaths of the outstanding women surgeons N.V. Almazova and Z.V. Vasilyeva. The former died after a minor operation from thromboembolism of the pulmonary artery. This is a complication which is practically impossible to foresee or to prevent, but Vasilyeva, who performed the operation, was so stricken with grief that she committed suicide. No wonder Sergei Yudin compared surgery with the highest form of art—tragedy.

A tremendous number of complaints boil down to a basic formula: "The patient died, the doctor is guilty." This is vicious and directly contradicts medical law. It is extremely rare that a physician exhibits carelessness in regard to the patient who entrusted his fate to the doctor; but if this happens, the physician is always punished.

Let us examine the reason why an oncologist may violate the dictum of Hippocrates to keep the patient unaware of his condition. This occurs when the patient himself must make the decision whether or not to consent to surgery. This decision carries much responsibility, possibly the greatest responsibility assumed in life.

There was an airline route over the hospital where one of the authors of this book worked for a good length of time. Whenever the airplanes broke through the sound barrier there was a thunderclap which made the windowpanes in the operating room resonate. Victories are usually marked by salutes, but some barriers are overcome quietly and without notice. There are the barriers that are registered in the case histories of patients by a routine phrase: "The patient has consented to surgery."

In making up his mind to undergo surgery, the patient hopes that the operating table will become the "watershed" on one side of which he will leave his disease and suffering, and on the other side of which he will regain his health and begin a new life. This seems all the more so, since the surgeon never expresses his doubts out loud. What if he should slip? Then the same problem may be viewed in another way: on one side there is life, no matter how bad, but still life, and on the other side, the dark unknown, even possible death.

At times one comes up against a deep contradiction: in suggesting that a patient undergo surgery after which he may become an invalid, the true diagnosis is concealed from him. The question naturally arises, If there is no cancer, why suggest such an operation? About a third of the oncological patients, who should undergo radical treatment, refuse to do so and thus doom themselves to very severe consequences. The following is an example of such a case:

Colonel F., 58 years of age, at first felt some difficulty in swallowing. He said nothing about this to his wife, a doctor, and his school-aged daughter, but he went to visit an X-ray specialist. The X-rays gave reason to suspect carcinoma of the oesophagus and he was advised to enter an in-patient clinic and undergo all the tests and prophylactic treatment. As often happens, the troubling symptoms passed, so the colonel, on comparing how he felt and the none too insistent recommendations of his doctor with all the house chores he had to attend to, decided to wait a bit. His wife was busy with her scientific dissertation, while his daughter was finishing secondary school. He waited until all these family events were concluded and appeared at the clinic only eight months later. The diagnosis was confirmed. This loss of time, however, led to the further spread of the cancerous disease and eventually to a tragic result.

The refusal of the patient to undergo surgery is at times tantamount to condemning himself to death. The reasons for refusing may be very different. One of them may be that the patient is not quite sure that he is really dangerously ill. This happens most often when the tumour is discovered accidentally during a prophylactic examination and has not as yet caused any serious suffering. This reason is directly reflected in the overall results of the cancer prevention campaign.

In Leningrad, during the last ten years, approximately one-third of all people discovered to be suffering from lung cancer by the simple method of fluorography and most (88 per cent) receive the diagnosis at a sufficiently early stage to be properly treated, but the mortality rate from this form of cancer, just as in the rest of the world, has not been substantially reduced. More than half of the established cancer patients diagnosed at an early stage, according to Dr. S.S. Yaritsyn, Chief Physician of the Leningrad Oncological Dispensary Clinic, refuse to be operated on.

Another example is from Japan, where morbidity due to carcinoma of the stomach is very high. Examination of the population was carried out on a mass scale using special optical instruments called gastroscopes. The examination revealed approximately 1000 persons in the earliest stages of the disease. These individuals had felt no symptoms as yet and it proved possible to persuade only half of them to undergo surgery. Incidentally, most of those who agreed to surgery were alive five years later. Those who had refused later came begging for an operation, but at stages when the symptoms of the disease were already very obvious. After five years less than a third of them had survived.

The authors have data documenting the refusal of patients suffering from carcinoma of the stomach to undergo surgery at various in-patient clinics in Moscow. As a rule, their disease was neither in an advanced stage nor complicated by any factors which suggests a favourable prognosis. Nevertheless, over 70 per cent of them died during the first two years after their release from the clinic. If they had been operated on, the reader himself no doubt realizes how different the results might have been. Refusal to undergo surgery for carcinoma of the stomach is tantamount to rejecting medical aid in general, because in this localization of cancer there are no other radical forms of treatment.

To clarify the reasons for rejecting surgery the authors polled a group of patients. The most frequent reason for refusal was fear. In many cases this fear was nurtured by witnessing the suffering of a neighbour in the ward who had been operated on, or by the fact that the patient himself was not feeling well or was already well along in years. Three patients explained that they had been "struck with fear" after a long wait for surgery. Two were afraid because the operation had been postponed several times.

Fighting fear, which, to quote one surgeon, is "the grey sister of pain", constitutes the principal task for both the medical personnel and for the relatives of the patient. Another reason for refusing surgery is because the patient has no complaints and feels quite well. Why is an operation necessary, if there is no pain? One 49-year-old lathe operator of the highest rank writes:

"When it becomes painful, you can cut me to pieces, but while I'm still normal, I won't be put on the operating table. It's not just a fingernail that will be cut, not even a finger, but my stomach."

Many patients refuse to be operated on because other forms of treatment have not been tried. Six of patients in the poll thought that a treatment method involving starving might rid them of cancer!

Some patients fear cosmetic defects. This is particularly true of female patients suffering from breast cancer, who are not yet advanced in age. They fear "the emptiness" that will be there after the breast is removed, although there are many ways (even reconstruction through plastic surgery) to conceal this defect.

To some extent all refusals by patients result from some problem in the relationship between patient and doctor, and at times deontological errors are particularly evident. Three patients, for example, refused surgery because the doctors had been arguing during their rounds. According to eight patients, the decision to operate had been too hastily made, without sufficient examination and preparation.

Among the reasons is also a lack of faith in the possibility of curing cancer. This is mostly found among patients with a fatalistic mentality after they have passed through many "hospital universities" and collected information exclusively of the reverse side of the coin. A sixty-year-old woman wrote, "I've seen more than enough suffering cancer patients in hospitals who come back to their cots with the same metastases." Another patient summed up his hospital observations as follows: "Those who were given chemotherapy lived less than a year, those who were operated on did not live even two years, those who were treated suffered pain, while those who refused treatment died a natural death painlessly..." It should be mentioned that the authors managed to persuade this not yet elderly man to undergo surgery. His stomach was operated on and he has already survived longer than the time he had calculated for such operated patients.

To overcome the barrier of refusal, the doctor must be absolutely sure, and the patient no less so, that there is no other way to regain health. The doctor gains such confidence through his knowledge and experience. In questionable cases he can arrange a consultation of medical specialists. What is more complicated in such a collision of sides is the most important factor—the patient who must be made to believe in the true inevitability of risk for the sake of saving his life. The patient has neither sufficient medical knowledge nor experience and this lends special importance to two factors: the authority of the doctor, and the opinions of relatives and the people surrounding him, which often prove to be more important than any consultations.

Ten of the polled patients rejected surgery under pressure from relatives. In addition, the authors received several letters requesting that they not psychologically traumatize the patient by reminding him of his severe disease, because he had no idea how serious it was. The proposed treatment, in the opinion of these relatives, carried no promise and was too risky. The following is an excerpt from such a letter:

"...receiving your letter from the oncological hospital was a shock for us and we consider ourselves fortunate that our sick relative has not seen it. Apparently, our concept of medical ethics is old-fashioned, but it is possible, though we doubt it, that a misunderstanding has occurred.

"The crux of the matter is that our father D. has never been told of the severe disease that interests you and we have spared no effort to keep him ignorant of this. His attending physician and the chief doctor of the hospital department where he stayed have, in all talks with him and in the certificate issued up on his release, mentioned only ulcer of the stomach and any reference to an operation was made only in this light. Moreover, if the issue was at first brought up very acutely and categorically, then the doctors of the hospital ultimately agreed with us in regard to the hazards involved in the surgery. On his dismissal they recommended a strict diet, general tonics, fresh air and so on. The hospital advised, and we put our trust in planned regular consultations with an oncologist, who could come to our home for the examination as an ordinary practitioner and, we hoped, in addition to all else, give us a prescription for sea-buckthorn oil. Father is now at our dacha in the countryside and we are doing everything to keep him well.

With due respect for the current interest in statistics we have done our best to reply to all the points in your questionnaire objectively. Please address us personally in regard to everything concerning father's treatment and please send letters with no return address by which he might learn of the nature of your medical establishment.

With our sincere respect and hope for your sympathy and understanding. Thank you for your kind attention and please forgive us for this letter..."

The letter needs to be commented on. In the first place it must be noted that in asking the patients these questions they were not informed of the actual diagnosis, but the questions were posed in a way that made them ponder, What is the real disease they are suffering from? This was not done accidentally. Analysis proved that just slightly over 15 per cent of those who refused treatment were aware of the seriousness of their condition.

Evidently, one of the main reasons for rejecting treatment is because patients have poor information of the nature of their disease. One cannot but agree with Academician N.N. Blokhin who contends that the refusal to be operated on because of disinformation due to deontological reasons "nullifies all deontological principles which hold the interests of the patient above all else".

Second, the questionnaires were distributed not just for investigative purposes, but also to try once again to force the patient to give more thought to surgery. This is why, among the questions, it was also asked whether the patient regrets rejecting surgery. Consultations were offered for those who desired to undergo surgery.

Twenty-nine patients said that they regretted their decision. Their replies showed how confused they were: "I'm up a blind alley." "I don't know what to do now." "I'm afraid, help me!" These patients were examined and nearly half of them were still at a stage when surgery was not too late. They were all successfully operated on and found hope for stable recovery.

As for patient D., whose relatives had sent the letter quoted above, his case history was reviewed once again and no absolute contraindications to surgery were found. The considerable risk, however, probably existed because of his age and that is why the doctors provided no guarantee. It is understandable why his relatives were so apprehensive, but unfortunately all that the authors can do today is offer their condolences. It is possible that if D. had agreed to an operation at that time, the outcome might have been different.

The spoken word is a powerful irritant and all the relatives and people surrounding the patient must bear this in mind. One of the authors of this book spoke with a young woman who was suffering from advanced breast cancer and suggested that her ovaries be removed. She timidly agreed, but the following day returned with her husband.

"Do you wish to castrate her?" he asked angrily.

"That is not the way we put it. We spoke of removing the ovaries."

"That means castration!"

The poor woman broke down in tears and absolutely refused to be operated on. It took a great deal of effort to persuade her to agree.

In 1975, J. Holland, an American psychiatrist who specifically investigates the psychological aspects of cancer affliction stated that the new level of evaluations of medical issues by non-professionals calls for a more complete explanation of everything connected with the disease, not only for the family of the patient, but to an ever greater extent, for the patient himself.

According to the data collected by many psychiatrists and psychologists, however, nearly all cancer patients who learn of their diagnosis experience the icy grip of fear, while nearly half of them are numbed by profound depression. Later they may develop a feeling of personal guilt or blame their relatives or their doctor for failing to prevent the disease. All this may give way to a defensive reflex: there develops either a refusal to believe the diagnosis, or an exaggerated faith in the doctor that he is absolutely capable of preventing the further development of the disease or of curing it. This natural reaction to the disease is like a symptom, just as, for example, the mania of persecution or litigiousness may be symptoms of specific afflictions of the brain.

Since 1950 American doctors have abandoned the practice of not informing the patient about his disease. The reason for this was not just because it was better for the health of the patient, which Professor Dan B. Dobbs frankly admitted, but also that the patient has the right to decide not because his decision may be the most reasonable one, but because it is *his* decision. The court defends not the health of the patient, but his right to decide his own fate...

To illustrate the point, the following is an excerpt from an article by Roy Rowan, a *Time* magazine reporter who related his reaction to the terrible diagnosis first pronounced by the surgeon: "You have a malignant melanoma," said the doctor distinctly, his black bulging eyes looking at me intently. I immediately took a liking to him. "Unfortunately, tumours of this kind have a tendency to spread," he continued. I imagine it is natural for a person to hear only what he wants to hear, because I thought he had said, "...do NOT have a tendency." I asked again and the doctor reiterated what he had said and calmly went on with his explanations. "The place where the tumour is located is rather hazardous. Analysis has revealed that the cells of the melanoma are in that state when they actively multiply and spread." He spoke evenly without the slightest show of emotion. This was a man whose profession called for dexterity, assurance and precise movements. The same qualities were evident in his manner of speech. He calmly proceeded to tell me what I should expect in the future.

"It is quite possible, that you are no longer ill. Maybe your operation was all that was necessary, but it is hard to say as yet whether or not this is so." At this point the doctor took out a silver fountain-pen and sketched a diagram of the operation he intended to perform on me...

"If the melanoma has not begun metastasizing," he said, "you have ninety chances out of a hundred to be cured...

"But if the melanoma has spread," he proceeded to the remaining possibility, "then your chances are nil." He then informed me of a statistical fact: "If the melanoma has reached the axillary node, the chances are fifty-fifty that it is advancing further."

It is very doubtful that informing the patient about the possible cause of the tumoral process helped him or made things easier. Although Rowan listened calmly and courageously, according to British psychologists, most patients prefer not to hear their doctor confirm the diagnosis of this severe disease with such a poor prognosis and, in any case, wish to retain hope for recovery; the more so, the information that the surgeon imparted to the journalist did not influence his decision regarding the operation and further treatment.

Incidentally, according to the report, the doctor further asked Rowan whether he wanted his axillary nodes removed or to leave them untouched. "He wanted me to decide the issue," remarked the perplexed journalist. This is also surprising because choosing a treatment is not the same as choosing a hairdo or clothing style.

According to S.S. Yudin, "...the surgeon must assume not only the risk that is involved; he must also decide for the patient the moral and psychological aspect of the case."

It is thus obvious that there are extremely different points of view as to what a cancer patient should know about his disease: Hippocrates represents the old approach and the Americans, as in one of the examples just cited, represent the new approach. The authors share neither one nor the other opinion. The truth, as it often happens, seems to be quite in between.

In some cases it is possible and necessary to inform what the diagnosis is, particularly if a curable patient resists complete medical treatment. Honesty, however, is not tantamount to cruelty by any measure. In being frank with his patient the doctor offers him emotional support and hope for recovery.

In other cases, particularly when radical treatment is impossible, the doctor is obliged to deceive the patient. Incurable patients stand in need to especially attentive care and encouragement both from the medical personnel and their relatives. One must play a role with them, day in and day out, without intermissions. This was done in a manner worthy of mention by Anne Philipe, the wife of the famous French actor Gerard Philipe, who died from a malignant tumour. In her memoirs *Le temps d'un soupir* she described how she succeeded in keeping her husband "in the dark" so that as his life ebbed away he did not know that he was on the threshold of death.

One must not yield to the doomed patient who insists that he be informed of the prognosis, asserting that he is strong enough to hear the worst, as long as it is true. As V.V. Veresayev once said, "If there is no hope, go ahead and lie to me until I no longer doubt that you are telling me the truth!"

Once the famous Soviet surgeon S. Mirotvortsev, while still a young man, was visited by his formed schoolteacher, who insisted on being told whether or not he was ill with cancer, and that if he was, how much longer he would live. He said that he had to know so as to put his unique library in proper order before he died. Mirotvortsev yielded to his pleading and informed the patient that he was ill with cancer and that he had approximately two to three months to live. A year and a half later the same old teacher came to see Mirotvortsev again. The surgeon was stunned, because he thought that he had died. They had a long talk which proved to be a lesson for life for Mirotvortsev. The schoolteacher told him that he had been leading a pitiful and miserable existence and had achieved nothing because the thought of his impending death completely absorbed his attention.

Even patients who are severely ill can be made to believe in the success of treatment if the doctor's behaviour and that of their relatives implies confidence. A fine illustration of this is seen in the case history of Nikolai Pirogov.

In 1881 the medical community of Russia celebrated the 50-year anniversary of the scientific and medical activities of its eminent surgeon. A stream of greetings and congratulations flowed to the small Ukrainian village of Vishnya where the "old doctor" (as Pirogov called himself in his *Diary* which he was writing at the time) lived. He was elected honorary member of countless medical societies and institutions; memorial wards and scholarships were inaugurated in his name.

Nikolai Pirogov had not experienced such a surge of enthusiasm and spirits for a long time. And everything would have been just fine if not for a small ulcer in his mouth which at times felt sore and bothered him. "Could this be the beginning of cancer?" Pirogov occasionally asked his wife but would chase the thought from his mind.

May 21, the culmination of his jubilee, was approaching when Nikolai Pirogov arrived in Moscow. He was named an Honorary Citizen of the town at this time and ceremoniously greeted at the University. The painter Ilya Repin asked the surgeon to sit for a portrait and Pirogov agreed. In the midst of all this celebration, he completely forgot about the ulcer and it was only on the third day after his arrival that he showed it to Professor N.V. Sklifosovsky. By this time, the ulcer had grown a little and the diagnosis left no room for doubt: cancer of the upper jawbone. A consultation of high-ranking experts decided that an operation was necessary.

The news traumatized Pirogov deeply. He could hardly sit through the luxurious banquet held in his honour at the Club of the Nobility and immediately after it was over he travelled to Vienna at the insistence of his wife and relatives to see the famous European surgeon Theodore Billroth.

On examining his patient Billroth sharply rejected the diagnosis and calmed Pirogov. Doctor S.S. Shklyarevsky who accompanied Pirogov on his trip recalled that, "Pirogov's spirits were immediately lifted and he rapidly changed from a depressed and doddering old man, which he had been all the way from Moscow to Vienna, to his formed young and vigorous self... Pirogov and everybody around him became happy and joyful again."

Billroth presented Pirogov with his photograph inscribed as follows: "to my dear and deeply respected teacher Nikolai Pirogov. The truth and full clarity in thoughts and feelings, in words and deeds are the steps of the ladder leading men to the divine being. My ardent wish is to follow your leadership, as bold as it was reliable, along this road, so often hazardous, shall always be my zealous desire,

Your sincere admirer and friend, Billroth."

On returning home Nikolai Pirogov reciprocated by sending his own portrait.

The high spirits and excellent mood caused by Billroth's categorical conclusion about the non-malignant nature of the ulcer remained with Pirogov practically until he died.

Had Billroth made a mistake in his diagnosis?

It has been established that Billroth knew the true character of the disease, but Pirogov's advanced years and the neglected stage of the process prevented him from proposing radical measures. "I doubt he could have survived an operation, and even if the outcome were favourable, it was more than probable that a recurrence would soon be expected," Billroth wrote to Dr. Vyvodtsev in Russia. Billroth used his unquestioned authority in order to give Pirogov hope for a favourable outcome and thus gave him peace at heart. "...I simply wished to distract the thoughts of the patient from the nature of his disease, and lend support to his firmness of will and patience... I acted as my duty and many years of experience prescribed..." he explained to Vyvodtsev.

Some contemporary authors abroad believe that a patient in an advanced stage of cancer should not be given reason for false hope. One can agree from the point of view that a flippant promise of rapid recovery is simply cruel, but it is no less cruel to adhere to the principles of ancient Indian medicine which only treated curable diseases. The hopeless patient was condemned to be drowned in the sacred waters of the Ganges. The heart of medicine is mercy and, if it is impossible to fundamentally help the patient, no effort should be spared to alleviate his suffering. Moreover, every new day brings new successes of cancer treatment and prevention.

In conclusion, let us cite William Faulkner's words on accepting the Nobel prize. In effect, he said that he refuses to accept the death of man, that man will not only survive, but triumph. Man is immortal not only because he alone in Nature has the invincible gift of speech, but also because he possesses a soul and spirit capable of compassion, sacrifice and survival...

The Authors Argue...

The careful reader may have noticed some contradictory judgements in this book. To some extent these contradictions may be based on objective factors that reflect the uneven accumulation of knowledge in such a rapidly developing science as oncology.

It would be risky to immediately and unconditionally transfer the results of an experiment to the clinic. It has been proved time and again that certain natural mechanisms discovered in animals were not confirmed in observations with patients. On the other hand, in the clinic it is extremely difficult to establish what the natural mechanisms are, owing to the immense variety of tumour pathology.

Breast cancer, for example, is a disease which has long been known and, unfortunately, is often encountered. Standard therapeutic approaches, however, have yet to be elaborated. This may be explained by the fact that there are seven stages of breast cancer occurring both in pre- and post-menopausal women. This totals to 14 variants. Also, there are at least five microscopic forms of cancer of this organ; therefore, the number of groups increases to seventy. If the results of treatment of even 1000 patients are available, no more than 15 patients can be allotted to each group, and if one considers several methods of treatment, the results of treatment will have to be compared between groups of 5-7 patients; this, to say the least, does not constitute a serious investigation. If one takes into account that one must wait for results for no less than 5 years, the reader will realize why there is no simple solution to this problem.

Under conditions of such objective difficulties, the subjective factor stands out prominently.

There are two authors of this book, two comrades in clinical work and research, close friends, but people of different age, temperament and destiny. One of the authors is already over sixty and has through the years seen the constant rise and fall of scientific theories. He remembers various sciences being branded and condemned, and periods when the true essence and meaning of what seemed to be ordinary medical problems were searched for and explored. He witnessed many large meetings at which representatives of different scientific trends were accused of numerous "sins". In spite of his generally optimistic view of life, he no longer believes in fashionable lightweight theories; he recognizes only solid facts and bows to the power of science. Let us conditionally label him the *Skeptic*.

The second author is younger. He has also traversed the long and arduous path of the practising physician. The difference in age, however, was favourable for the scientific maturity of this author, in the sense that he took up scientific studies after all distortions and mistakes had been corrected. Therefore, it was easier for him to assimilate scientific theories and success gave rise to optimism. So, let him be called the *Optimist*.

Optimist: Don't you think that the symbolic award for the best definition of the concept of cancer, which two centuries ago was conferred upon Bernard Peyrilhe, should be given to Academician L.M. Shabad? It's a good thing that our science is advancing from agnosticism and negativism ("Cancer is a disease which is just as difficult to define as it is to cure.") to the penetration of mysteries and control over them ("... cancer as a pathological process is dedifferentiation and the multiplication of the cells of the organism, which pass this property on to daughter cells.").

Skeptic: The formulation is profound but far from all-embracing. L.M. Shabad added to it by saying that cancer is not one disease, but many diseases combined in one concept. If this is so, there can be no question of any victory in this contest because it is impossible to combine 200 different diseases under one definition.

Optimist: But why? We use the term cardiovascular diseases, although among them we include infectious, allergic, congenital diseases and so on.

Skeptic: Yes, but in this instance the diseases are grouped according to the organ they affect, by the anatomical location of the process, whereas cancer strikes the most different locations and, in each of them, it is different. Together we counted more than 70 forms of breast cancer alone. Is it possible to embrace the unembraceable with just one formula?!

Optimist: The more we learn about cancer the harder it is to keep within the framework of the definition. Is there any need for this, anyway?

Skeptic: Of course there is! Otherwise how can we explain what cancer is? The skeptical attitude in oncology is founded on the inability to provide a sensible reply to this question. It turns out that we wrote a book about nobody knows what...

Optimist: How about this: Cancer is a term under which we mean a group of diseases (like the term "mental diseases"). They are of the same essence, there is one common sign—unrestrained progression—although their origin may be different.

Skeptic: I agree. I only wish to emphasize that this constitutes the basic objective problem in studying the group. It is generally believed that to make correct diagnoses and elaborate proper therapeutic and organizational measures one must, before all else, have a proven theory of the origin and development of malignant tumours. Without such a foundation there can never be any reasonable system for preventing the causes and improving the health of our patients. This means that we cannot expect any particular successes.

Optimist: I never thought your skepticism would outweigh your knowledge. There are two refutations. The first is that the chosen practical measures far from always followed the discovery of the nature of the disease. The second is that the experience accumulated to date provides sufficient grounds to work out an effective strategy and tactics. Just recall the replies that prominent oncologists in their time gave to one of the questions in our poll, namely, "Is there any hope that in the twentieth century there will be a proven theory of the aetiology and pathogenesis of malignant growth?" Academician A.I. Serebrov answered, "It is impossible to work without hope!", and Professor Sh. Ekhardt replied, "The current state of science and the results which have been scored in oncology provide us with hope."

Skeptic: Let us examine this in greater detail. Hope is not the factor which helps the practitioner who is confronted by a cancer patient. Let's try and sum up the facts so we can get down to earth and tackle our immediate tasks.

Optimist: Before all else I wish to prove that knowledge of the origin of the disease is not a "must" for successfully preventing and curing it, although such knowledge, of course, makes this task much easier. Nonetheless, at the end of the eighteenth century the British physician E. Jenner found a method to prevent viral smallpox, to the immense benefit of mankind. It is a curious fact that the first institute of smallpox vaccination (later named after Jenner) was founded in London as long ago as in 1803. At the time nobody knew anything about viruses; hardly anything was even known about microbes. Louis Pasteur, the founder of microbiology as we know it today, was born 19 years later (in 1822).

Skeptic: You are right! Moreover, a knowledge of aetiology is still not the solution to the entire problem. Take tuberculosis, leprosy or the plague. Many decades passed between the time their causative agents were discovered and effective methods for their prevention appeared. As for tuberculosis, a disease with obviously social features, Calmette-Guérin vaccine, just as the contemporary system of drug, surgical and balneological treatment, failed to overcome it. Large-scale social measures proved necessary to solve the problem of the complete eradication of tuberculosis in the highly developed, primarily socialist, countries towards the end of the twentieth century. It is from such facts, which confirm your premise that there is no direct dependence between the successes of theory and practice, that my skepticism stems.

Optimist: We are going back and forth as if we were on a swing! Either I am right, or the next moment, you are! I think we are both right. There are grounds for skepticism, but absolutely no grounds for pessimism in assessing the situation. Just look at how much is already known and how much has been achieved!

Many theoretical discoveries have been made concerning the specific structure and function of tumour cells: the production of embryonal protein, the loss of contact inhibition, the fundamental reversibility of tumoral transformation, the participation of immunological mechanisms in the development of tumours and so on.

A theory has been elaborated about the progression of tumours, permitting us to comprehend their boundless variety as a manifestation of a regular mechanism.

The significance of chemical and physical factors has been proven for the origin of many types of tumours and this formed the basis for developing and applying effective methods for the prevention of "occupational cancers".

The role of viruses in the formation of certain malignant tumours is being intensively studied. It has been clarified how the endocrine system of the organism behaves during the tumoral process.

And lately, successes have been scored at the intersection of genetics and oncology. But this is far from all.

Skeptic: The sum total of theoretical research, however, does not give much hope for optimism. It can only be stated for sure that cancer can be induced in animals by a great variety of methods. We have yet to learn whether there is any single pattern in the kaleidoscope of theories.

Optimist: A scientist once said that a hypothesis refuted by new facts dies with honour. The accumulation of data presumes the inevitable transition of quantity into quality. I have no doubt that the time is not far off for the birth of an integrative theory of cancer which will have practical value.

Skeptic: The complexity of the problem lies precisely in the circumstance that in the first place the time has not yet come for a generalizing theory and, in the second place, practically every scientist who has gotten some kind of result is inclined to consider his efforts as having been made "in the only right direction". It depends on his scientific conscientiousness as to how he will declare his position. Those who are less modest loudly proclaim that they have solved the problem of cancer; those who are more modest say that they have developed a unifying integrative theory.

Optimist: Let's not cavil at every word. Science is created by people and everyone wishes to be worthy of the golden monument which, according to legend, will be erected to the man who conquers cancer.

Skeptic: I'm afraid the computer will get the golden monument considering the infinite volume of rapidly accumulating experimental data and clinical observations. Incidentally, Süss, Kinsel and Scribner tried to formulate the problem of cancer for the computer. As far as I know none of the mathematicians took to the idea. It is probably too early as yet.

Optimist: I remember their formulation. It was interesting in that it very aptly summed up everything that is already known about tumours. We can use it to review the basic data.

Thus, the three main stages in the development of a tumour are: transformation, activation and progression. Transformation (the malignant transformation of the cell) may occur for many reasons: the effect of a physical or chemical carcinogen, a virus, and so on. Let us take the case of a chemical carcinogen which encounters a normal cell and penetrates it. The defense mechanisms at the cellular level (enzymes) may split and oust the carcinogen, which occurs most often. Sometimes the carcinogen manages to interact with the DNA (hereditary material) of the cell nucleus. The reverse development of the process is also possible if "cleaners"—the repair enzymes—interfere. If this does not happen, the cell transforms, but not into a tumour as yet, just into its real prerequisite.

The stage of activation ensues. The

transformed cell starts to reproduce and if it manages to "escape" from the organism's regulation of division (connections with other cells are disrupted and inhibition signals are ignored) a pathological clone is formed. The growth of this clone is also hampered by several obstacles, the most important may be the immune defense system. If this "does not work", the transformed cell may become a tumour cell. As you see, there are many obstacles along the path of the malignant tumour! This is precisely why cancer is a comparatively rare disease.

Next comes the stage of progression. Under the influence of the reactions of surrounding tissues, hormones and several other factors, a tumour forms which penetrates into neighbouring organs and produces metastases.

Incidentally, this chain of events predetermines the effect of local treatment in early stages of cancer and the need to apply overall methods when the tumour progresses.

One of the outstanding successes in oncology is the well-organized and very effective system in the USSR for preventing and treating malignant tumours. It is being constantly improved.

During the last thirty to forty years many operations have been performed which formerly had seemed fantastic for carcinoma of the lung, oesophagus, the upper third of the stomach, pancreas, and many other organs. In the thirties and forties, as many oncologists remember, such cases were considered incurable, but now tens of thousands of these operations are very successfully carried out every year.

Skeptic: Far from all of them are successful...

Optimist: That's true, but the problem is not in the methods of treatment but due to other causes which we have discussed in this book. Allow me to finish enumerating our successes and then we can return to this question.

Special medical apparatus have been designed for irradiation with beams of high energy and radioactive isotopes. The field of drug therapy is being expanded.

Immense research is being carried out to provide the theoretical foundation and clinically apply methods of immunotherapy...

Skeptic: Don't you think this last point is still very doubtful? Is there any proof of anti-tumoral immunity?

Optimist: Of course there is! Many volumes have been written on the subject.

Skeptic: At the beginning of 1980 a book was published in the Soviet Union written by the eminent French specialist in oncology and immunology Mathé. In the book the author poses three questions:

(1) are immune reactions capable of destroying tumour cells?

(2) do cancerous cells carry special antigens?

(3) can we possibly control the mechanism of immunity in such a way as to make it kill a greater number of cancerous cells than it does under natural circumstances?

Mathé gave a positive answer to all three questions and then cited the results of experiments which seem to confirm this point of view.

Optimist: There you are! Probably this is precisely where the answers lie; it is most important because we will be promoting activation of the natural and, therefore, the most reliable, method for protecting the organism from cancer.

Skeptic: Don't rush! Further, Mathé writes that the sparse data we now possess concerning *human tumours* are too complicated for interpretation. According to Mathé, one may presume that for some tumours one or several antigens have already been discovered or are being studied from this angle. Don't you agree, it's not very convincing?

Once, at a scientific meeting, Professor G.I. Abelev replied to my blunt question that they are most likely not true antigens, but just "markers" of tumours, that is, protein substances testifying to the presence of a tumour and the shifts that it causes.

Optimist: Nevertheless, there has been definite progress in this field. Just recall immunotherapy for leukoses in children, successfully applied by V.M. Bergolts and N.A. Kislyak, or the successful observations made by Mathé, V.I. Govallo and N.N. Trapeznikov.

Skeptic: Let us settle on this: the study of the immunology of tumours is of great interest, but as yet has not advanced beyond the limits of specialized research and clinical institutions. Immunology has not yet won the right to be called an integrative theory, and the efforts that have been expended so far have not produced adequate results.

Optimist: I feel obliged to yield to this gloomy conclusion. I would like to add a joyous note, however. In recent years a clear-cut connection between genetic and immunological mechanisms has been established. In particular, in several thousand very complicated experiments on mice conducted under specific conditions of "genetic purity", with very strict genetic control, Snell established that certain groups of genes carry a very definite responsibility for the immunological reactions of the organism. For example, he proved the dependence of the rejection reaction in organ transplants on a very definite group of genes. The same genes control the ability of the organism to resist diseases.

The theoretical finding called for confirmation by direct experiment which could only have consisted of the following: to remove the gene from the DNA helix and produce an animal without the function that the gene was responsible for. Three scientists, P. Berg, W. Gilbert and F. Sencher, developed a technique for the recombination of genes, i.e., different DNA fragments are split and transplanted from some animals to others on the basis of the rapid determination of the exact sequence of nucleotides in the given DNA molecule.

On the basis of all these outlined theoretical and methodological steps, Jean Dausset proved that it is precisely a definite group of genes which determines the success of organ and tissue transplants, and that the tissues of every individual (except uniovular twins) are in themselves unique. B. Benacerraf further refined the theory in experiments on guinea pigs which established that *one* dominant gene is responsible in the organism for defense against bacteria and viruses. The Nobel prize was awarded to all of these scientists in 1980.

It may eventually turn out that immunological reactions, the entire system of immunological defense, is only the executive apparatus of more complicated defense systems that include many components very closely interconnected with one another and mutually regulating. We hope that anti-tumoral defense is also located somewhere in this system. Incidentally, in scientific forecasts (by 1990 A.D.) a prominent place is allotted to immunoprophylaxis and immunotherapy. By that time it is hoped that methods for the immunological treatment of the tumour cell, as well as for vaccination to prevent relapses after treatment, will be elaborated.

Skeptic: Let's hope we'll live to see that day. But if you are right, we are not at the road's end of investigation, but at the very beginning of a thrilling scientific detective story. Can patients hope for a happy end, though? Every day people continue to die of cancer.

Optimist: Don't be so gloomy! Every human is fated to die in the long run. Nobody has as yet secured a pass to immortality. I'll remind you of a cynical joke made by an old doctor. When a patient asked him if he would die, the physician immediately replied: "Without a doubt." And then after a pause, "But not too soon and not from this disease."

To be sure, people practically no longer die from epidemics. Even children with severe forms of congenital heart disease, who were expected to die, now live to a grand old age, and so forth. Thanks to the successes scored by medicine and to social progress, the human life expectancy is increasing and, therefore, there is a greater hazard of reaching the dangerous age when malignant tumours usually develop. It is common knowledge that cancer is for the most part a disease afflicting the elderly.

Skeptic: You were right in saying that it's not cancer that occurs more often now, but that more people live to the age when cancer is likely to strike.

Optimist: Roughly speaking, this is so. The mortality rate resulting from cancer has increased in these last hundred years, but we must remember that we do not know what the situation was in past times. There was no accurate documentation of cancer incidence in our country before the 1940s, and such records do not exist in some countries to this day. In countries where statistics are reliable, such as in the USSR, it is seen that increases in incidence during the last twenty years are not very great. The same statistics testify indisputably of the considerable gap between the number of registered cases of the disease and the mortality rate. This means that we must take into account the increased skill of physicians who manage to detect and cure cancer patients, as well as the continuous improvement in methods of cancer prevention. This has been described in detail in the book.

Skeptic: Let us return to the problem of cancer incidence. One question is still not clear. In the USA at the end of the sixties the Terry report was published which investigated mortality due to cancer in America between 1900 and 1960. The population of the country more than doubled in this time. It would seem that deaths from cancer should also have doubled, but they did not. They increased eight times (from 3.3 to 20.9 per cent). Could this be due to the "ageing" of the population? Let us look at the figures. In 1900, 7 per cent of the USA population was over sixty; in 1960, this figure rose to 14 per cent. Another doubling. Such a cause as the increase in life expectancy fails to account for the surplus of oncological diseases by a third. The presence of this substantial excess allows one to assume that there must have been some other causative factors which accumulated. The fact that this same picture is found in all the industrially developed countries provides grounds for reflection and skepticism.

Optimist: I fear you are straying from the point in question. Rather, the formal incidence is greatly influenced by the state of statistics. In 1900, the system of registration was incomparably worse than in 1960. Couldn't there have been a statistical increase of the incidence instead of an actual increase?

Skeptic: I must agree that there is some truth in what you say. In this book we wrote, and this is true, that only a diagnosis confirmed by laboratory tests can in the long run be believed. We prescribe radiation and drug therapy only if we have a histological analysis. Statisticians, however, base their figures on the conclusions drawn by physicians regarding the death of their patients, without delving into other documents including autopsy reports. Their generalizations are not always exact. Nonetheless, if we look at more contemporary periods of time when the sources of information were of the same type and the mistakes were probably much the same, it is not difficult to see that there really was an increase in malignant diseases.

Optimist: We are taking a much too narrow look, forgetting about the general picture of diseases. Cancer does not frequently occur. Every year 30 million infants in the world die from malnutrition and infections, 10 million adults die from tuberculosis and malaria, another 10 million from other causes including traumas, 5 million from cancer and another 5 million from cardiovascular diseases. In the clinical practice of a British doctor who treated 2500 patients (statistics from Dr. Fry), the doctor encountered cancer a hundred times less frequently every year than pneumonia. The same number of people suffered from myocardial infarction, haemorrhages in the brain and tumours. Moreover, myocardial infarction and stroke are no less hazardous than cancer. Why does cancer cause so much fear?

Skeptic: Probably because we really help far from all cancer patients. We make no secret of the fact that some patients die even after radical treatment, both in early periods from complications, and in later periods, from recurrences and metastases.

Optimist: This is connected with the late detection of the disease. The earlier the tumour is diagnosed, the more chances there are for recovery. This natural law is true not only for cancer. Nobody fears appendicitis, for example, but unless it is diagnosed in good time, the purulent condition will progress. Thousands of people to this day die from peritonitis, but for some reason neither peritonitis, tuberculosis, dysentery, nor even infarction give rise to panic, whereas cancer is perceived as something fatal and causes such alarm that it has been dubbed "the disease of the century".

Skeptic: This is greatly due to the fact that we often conceal the actual disease from the patient and sometimes from his relatives, and people are apt to fence off any truth, especially if it is an awful truth.

Not everything that is good for one person is good for everyone else. If a patient has been cured of cancer, he and the people around him never know what he was sick with, as a rule. If the patient died from cancer, relatives, friends, neighbours and practically the whole neighbourhood knows about it. It matters less that he died than what he died from. Nobody bothers about the details: Cancer! That is all there is to it! This is why the delusion of one person, one family, deludes many other people, distorts public opinion about the hazard of malignant tumours and gives rise to doubts as to the efficacy of modern treatment.

This is a major cause for the attitude about cancer nurtured among the population. This is not the only reason. Also, the last most tragic period in the life of the incurable cancer patient is witnessed by his relatives if he dies at home, or by his neighbours if he dies in a hospital.

Optimist: It is indisputable that, among the complex of enumerated causes, the last is the most illustrative. Take, for example, the way that dying people are represented in different books. How did people die from consumption in K. Fedin's and E. Remarque's novels? Till their last breath they walk around, converse with others and do not particularly suffer from pain. Feeling not quite well or having a fever is usual for them, whereas the cancer patient suffers from severe, at times humiliating, pain. I must say that today a lot is being done to make the lot of this category of patients easier (anaesthesizing drugs with long-term effect, psychotherapy, special care and so forth). The principal factor, however, is the tremendous work undertaken to detect cancer in its early stages; this effectively "redistributes" patients according to the stage of cancer that they are suffering from, and sharply reduces the number of individuals in the fourth clinical group. If you will recall, in 1903, as the first in Europe, the Moscow Oncological Institute was founded mainly to "provide charitable care for cancer patients". Only charity and mercy could ease the suffering of up to 90 per cent of patients at that time; whereas now, less than one-fifth are in such advanced stages. That is real progress!

Skeptic: I do not doubt that progress, but public opinion is hard to change. I imagine that "fashion" is also to blame here. It is currently in vogue to speak of cancer and claim that doctors are no good and no successes have been attained.

Optimist: I think things are not so gloomy as you make them to be and that there are already quite a few people who have faith in the possibilities of medicine, otherwise there would not be such an influx of visitors to oncological clinics for examination. Fortunately, only a small number of those referred to the oncologist or coming voluntarily have been found to have cancer. Since people come to us, doctors, that means they have faith in us, and the better we work, the more patients we cure and faster people develop trust in oncology and lose their fear of malignant tumours.

Skeptic: There can be no doubt about this, nevertheless, I wish to emphasize that people are still afraid and mistrust is still there, nor has the "nutritious soil" for quacks and miracle workers disappeared.

Charlatans and "healers" are agile in filling the vacuum of information and are clever in advertising their "skills". Rumours of their miraculous cures spread like wildfire among the population.

Optimist: Although we have already written much about the harm caused by charlatans and should, I think, have convinced the most prejudiced reader, it is essential to emphasize once again that this has grown into an international problem so that many scientists and practitioners are obliged to keep on grappling with it. In her book *Le cancer*, S. Laborde, the famous French oncologist and popular science writer, notes that the patient who runs for help to a quack is a lost man, because he cuts off all ways to radical treatment. It is also very hard to convince people that there are no undiscovered "secret" medicines.

In view of this, the oncologist's position in regard to non-professional methods for influencing patients must be firm and resolute. Any other behaviour or attitude is a mistake and is harmful because it also harms medicine, undermining its authority. The wrong attitude may and often results in the patient's refusal to submit to proper treatment, instead he runs to the "healers". This most likely occurs with cancerous patients who can be cured, but who thus sign their own death sentence.

Skeptic: Many years will pass before such people will be dissuaded and such doctors educated to act as they should.

Optimist: The daily selfless labour of our medical colleagues must and shall lead to success in curing cancer and in significantly improving the moral climate surrounding oncology. This book is but a small contribution to this tremendous cause.